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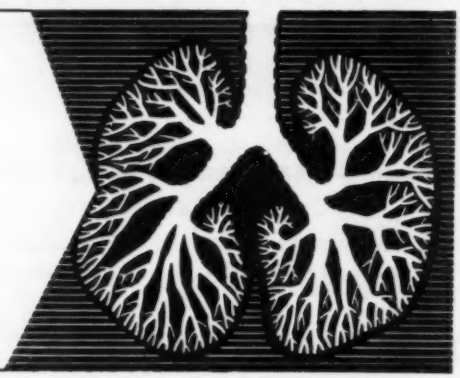

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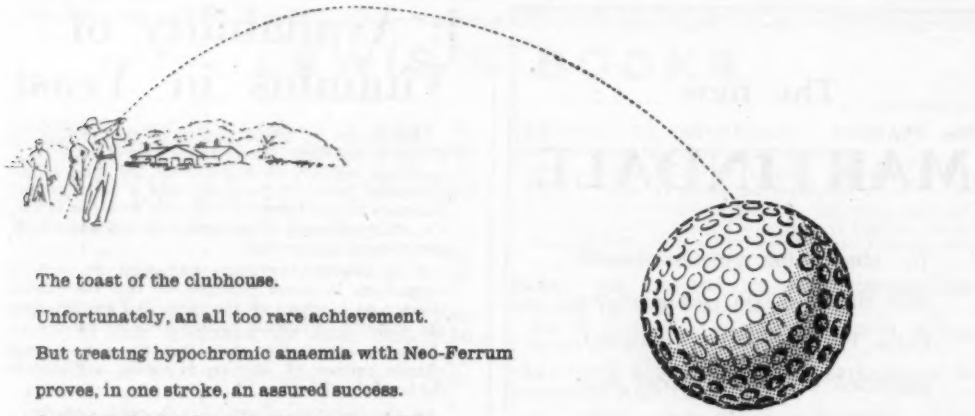

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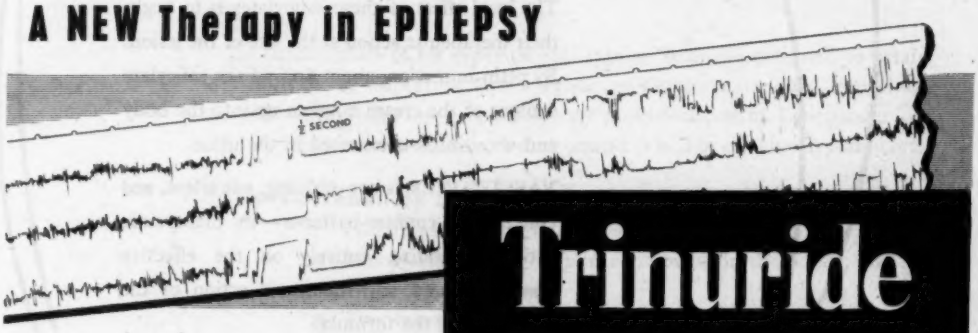


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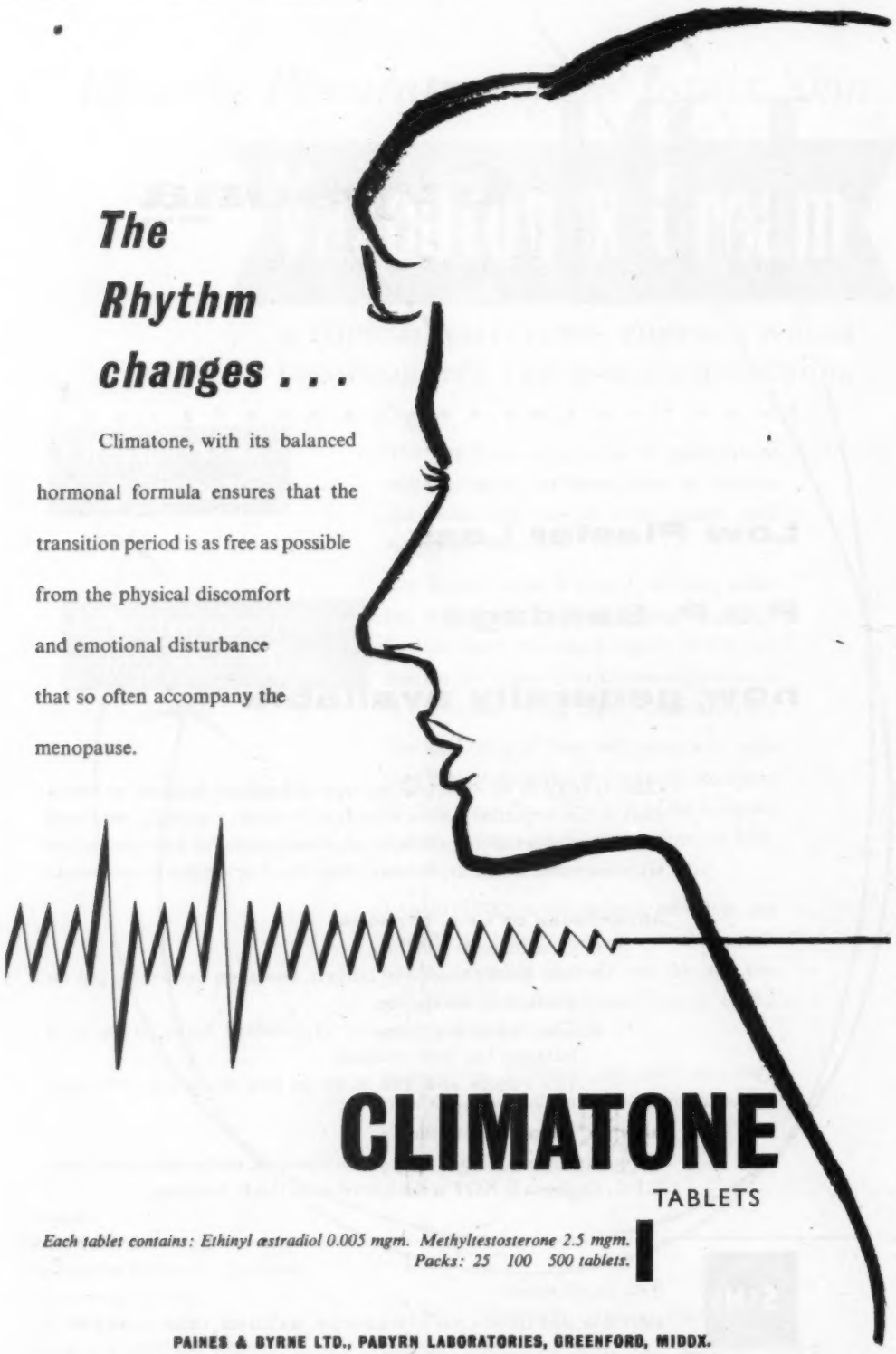

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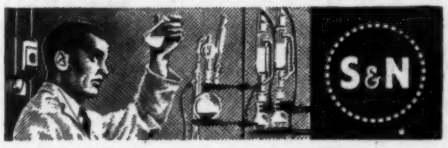
**PAINES & BYRNE LTD., PABYRN LABORATORIES, GREENFORD, MIDDX.**

When Calcium B-P.A.S. or isoniazid is called for

THERAPAS or PYCAZIDE

AVAILABILITY
**THERAPAS** (*calcium B-P.A.S.*)
Packets: 3·5G. Cachets 1·0G.
**PYCAZIDE** (*Isoniazid B.P.*)
Tablets: 50 mg. 100 mg. Ampoules: 50 mg. in 2 ml.
Syrup (*blackcurrant flavoured*): 20 and 80 fl. ozs.

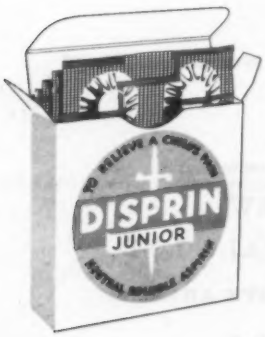



'Specialists in tuberculostatic drugs'

*Literature and dosage charts on request to*
SMITH & NEPHEW
PHARMACEUTICALS LTD.
WELWYN GARDEN CITY · HERTS.

# New – DISPRIN JUNIOR REGD.

## Disprin is now available in a children's size tablet containing 1·25 grains of aspirin in soluble form




Disprin Junior is so suitable for children because:
it is soluble
it is easily administered, dissolved in water
it is sufficiently palatable

*Formula:* Acid Acetylsalicyl B.P. 1.25 gr., Calc. Carb. B.P. 0.375 gr., Acid. Cit. B.P. (Exsic.) 0.125 gr., et excip.

*Patients can obtain Disprin Junior at all chemists, in cartons of 16 tablets in airtight foils, price 9d. inc. P.T.*

RECKITT & SONS LTD., PHARMACEUTICAL DEPARTMENT, HULL

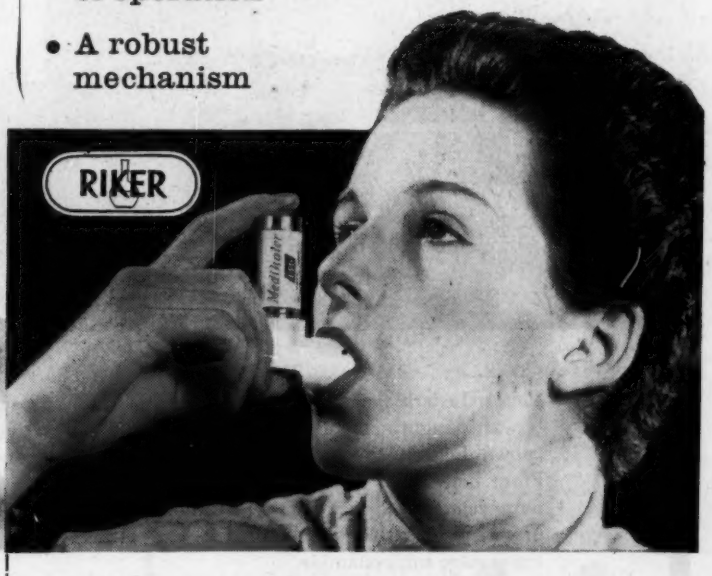
NEW

# THE RIKER 'Medihaler' REGD.

## The most significant advance in recent years in oral inhalation therapy for asthma

**THE 'MEDIHALER' PROVIDES THESE UNIQUE FEATURES**

- A measured dose of predetermined particle size
- An aerosol spray mechanism
- Extreme simplicity and ease of operation
- A robust mechanism




**'Medihaler EPI'**

Contains 7 mg./c.c. Adrenaline Acid Tartrate B.P. in suspension in inert aerosol propellent. Dose delivered is equivalent to 0·15 mg. adrenaline base.

**'Medihaler ISO'**

Contains 2 mg./c.c. Isoprenaline Sulphate B.P. in inert aerosol propellent. Dose delivered is 0·075 mg. isoprenaline sulphate.

**PRESCRIPTION INFORMATION**

The first prescription should order a Complete Outfit of either 'Medihaler Epi' or 'Medihaler Iso' (propellent unit and oral adapter).

The basic N.H.S. cost is 12/8d.

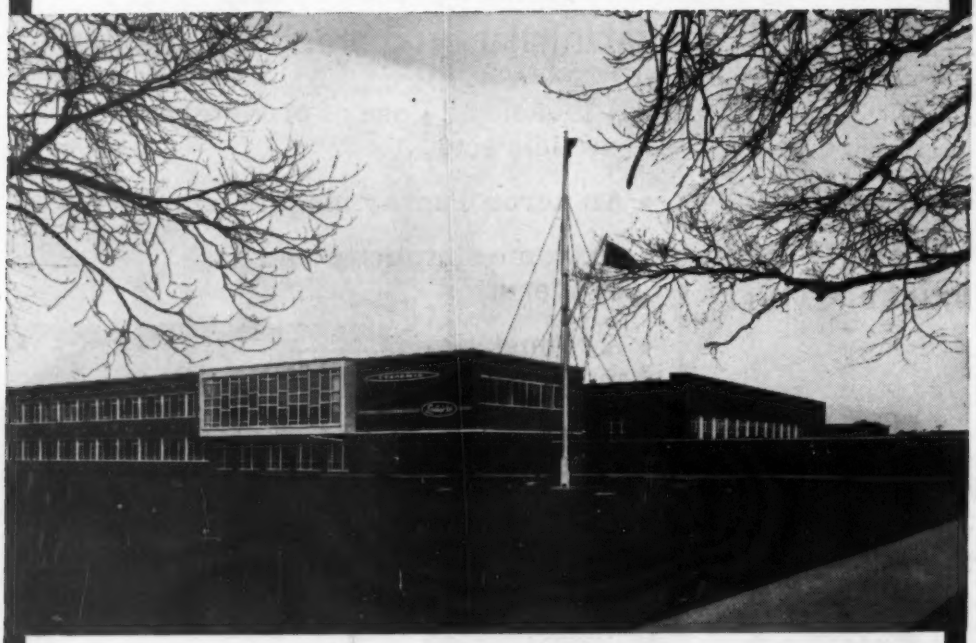
Repeat prescriptions should specify the appropriate refill propellent unit required.

The basic N.H.S. cost is 10/4d.

'Medihaler' is a registered trade mark.

**RIKER LABORATORIES LIMITED**
**LOUGHBOROUGH · LEICS.**

# BUILDING for a better world



This is Lederle's new pharmaceutical plant at Gosport, Hampshire. It was inaugurated this week and is now in full production of well-known Lederle drugs that are helping doctors to conquer disease. From here come AUREOMYCIN* chlortetracycline and ACHROMYCIN† tetracycline—leaders among the antibiotics . . . LEDERCORT†—Lederle's new corticosteroid of great promise . . . LEDERKYN† —long-acting, low-dosage sulphonamide.

Lederle is a branch of the vast international Cyanamid organisation, and leadership in pharmaceutical research is but one of Cyanamid's contributions to a better world. In other fields too—industrial chemicals, plastics, agricultural products, food preservation, surgical products, etc. the latest news is often of another Cyanamid achievement that transmutes the hopes of yesterday into the realities of today.

*TRADEMARK †REGD. TRADEMARK

Lederle

LEDERLE LABORATORIES DIVISION

*Cyanamid* OF GREAT BRITAIN LTD., London, W.C.2

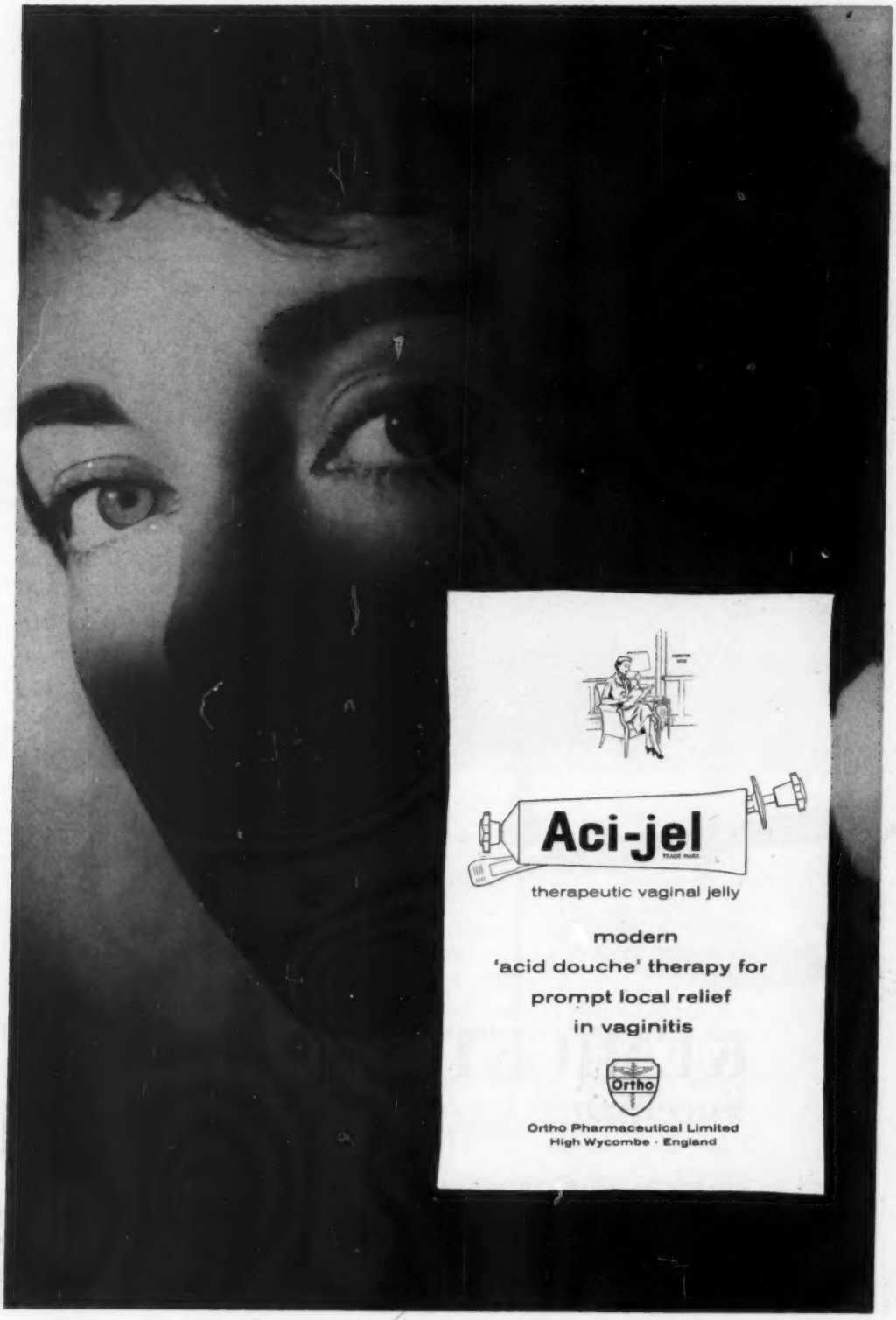
*Increasingly wider use*

*Carlo Erba presents the first lyophilyzed water - soluble chloramphenicol, Kemicetine Succinate, thus making possible the parenteral administration (intravenously, intrathecally, intrapleurally, etc.) of this antibiotic and greatly increasing its range of application.*

KEMICETINE
Succinate

Water soluble

CARLO ERBA MILANO


Aci-jel
TRADE MARK
therapeutic vaginal jelly
modern
'acid douche' therapy for
prompt local relief
in vaginitis
Ortho
Ortho Pharmaceutical Limited
High Wycombe · England

# Better relief for arthritics—minimum side effects

In salicylate therapy BUFFERIN (Antacid Analgesic) has these two special advantages. It is *faster-acting* — twice as fast as ordinary aspirin. It is *better tolerated* — even in large doses, as for arthritis.

According to a British survey, as many as 42% of arthritics are intolerant to aspirin. And in a blind trial among arthritics with a *proved* intolerance to aspirin, 70% had no gastric symptoms after taking large doses of BUFFERIN over periods of 4 to 16 months. (1).

In clinical tests, it was shown that BUFFERIN raises the salicylate blood level of humans more than 20% higher in *ten* minutes than ordinary aspirin does in *twenty* minutes.

Hence the importance of BUFFERIN in all salicylate therapy. Only BUFFERIN contains the antacid agents which :—

* reduce gastric upset to a negligible minimum (2), (3);
* actually speed the pain-relieving ingredient into the blood-stream (4), (5).

**IT ACTS FASTER. IT IS BETTER TOLERATED. IT CONTAINS NO SODIUM.**

1 (*Bufferin in the Management of Rheumatoid Arthritis, J.A.M.A. 158:386 (June 4) 1955.*)

2 (*The Neutralization of Gastric Acidity with Basic Aluminium Aminoacetate, J. Pharmacol. and Expera Therap. 82:247 (Nov.) 1944.*)

3 (*In Vitro Differences Between Dihydroxy Aluminium Aminoacetate and Dried Aluminium Hydroxide Gel, J. Am. Pharm. Assoc., Sc. Ed. 41:361 (July) 1952.*)

4 (*Effect of Buffering Agents on Absorption of Acetylsalicylic Acid, J. Am. Pharm. Assoc., Sc. Ed. 39:21 (Jan.) 1950.*)

5 (*The Pharmacologic Principles of Medical Practice, ed. 3, Balto., The Williams & Wilkins Company, 1954, p. 593.*)

*Formula: Acetylsalicylic Acid 5 gr: Aluminium Glycinate ½ gr: Magnesium Carbonate 1½ gr.*

**BUFFERIN HAS NO EQUIVALENT IN THE B.P. OR NATIONAL FORMULARY.**

# BUFFERIN

*is the trade mark of the Bristol-Myers Co. Ltd., London and New York.*

*Sole distributors in U.K.:* J. C. Gambles & Co. Ltd., 209-215 Blackfriars Road, London, S.E.1.

*Bufferin is now available in the Irish Republic—sole distributors:* Messrs. Fasset & Johnson (Ireland) Ltd., 6-7 Crow Street, Dublin.

*Please write for free samples to:* BRISTOL-MYERS COMPANY LTD., 209-215 BLACKFRIARS ROAD, LONDON, S.E.1.

# Two in harmony

THE TWO active ingredients in 'Sulmezil' V perform together *in harmony*. Together they are much more effective than either used singly.

One ingredient is penicillin V, the acid stable form of penicillin which is rapidly and efficiently absorbed and gives consistent and reliable blood levels. This form of penicillin has proved to be markedly superior in these respects to other oral penicillin preparations.

Combined with penicillin V is 'Sulphamezathine', which has been widely accepted for many years on account of its high potency coupled with low toxicity. It is undoubtedly the best sulphonamide for routine use.

'SULMEZIL' V TABLETS
Packs of 25, 100 and 500. Each tablet contains 60 mg of penicillin V (Calcium Salt) and 0.5 G of 'Sulphamezathine'.

'SULMEZIL' V SUSPENSION
Bottles containing 2 fluid oz. when dispensed; each fluid drachm of the prepared suspension contains the same dosage as the tablets.

**'Sulmezil' V**

**TABLETS AND ORAL SUSPENSION**

IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

Ph. 747/1

# a complex need

STRENGTH?

LOTION?

OR OINTMENT?

GREASY?

OR NON-GREASY?

# a simple answer

**CORTRIL TOPICAL OINTMENTS**

Greasy: 1.0% and 2.5%.
Non-Greasy: 0.5%, 1.0% and 2.5%.
Both in tubes of 5 g. and 15 g.

**CORTRIL LOTION**

0.5% and 1.0%
in 20 ml. bottles.

**Cortril***
brand of hydrocortisone

***IN ALL NON-INFECTED DERMATOSES***

**PFIZER PHARMACEUTICALS**
*Manufactured at Sandwich and Processed at Folkestone, Kent*

* *Trade Mark*

Pfizer

072/P

# PREDICTABLE *ANTACID THERAPY*

**PRODEXIN**

1 **rapidly relieves gastric pain**
2 **safely buffers excess acid**
3 **non-alkalising**
4 **non-constipating**
5 **stable, consistent and predictable**

Prodexin tablets sucked regularly provide continuous buffering of gastric acid at about *p*H 4, in the face of widely differing acidities and irrespective of the rate of emptying of the stomach. Prodexin does not make the stomach alkaline and does not stimulate compensatory secretion of acid. The tablets are pleasant to take, non-gritty and non-constipating.

**PRODEXIN**

**Each Prodexin tablet contains:**

Aluminium glycinate (dihydroxy aluminium aminoacetate)..... 0·9 gramme
Light magnesium carbonate..... 0·1 gramme

*Cartons of 30 singly wrapped tablets.*

*Dispensing packs of 240 tablets (basic N.H.S. cost 30/4d.)*

601/6013

**C. L. BENCARD LTD.** · PARK ROYAL · LONDON · N.W.10

# The esters of NICOTINIC, SALICYLIC and p-AMINOBENZOIC acids

## bring relief to cases of arthritis and rheumatism

IN CASES of soft-tissue rheumatism, and arthritic disorders, many doctors are tending more and more to regard Transvasin as an indispensable adjuvant to treatment.

For Transvasin is composed of the esters of nicotinic, salicylic and p-aminobenzoic acids. These esters readily pass the skin barrier in therapeutic quantities, and so enable an effective concentration of drugs to be built up where they are needed.*

Transvasin not only induces vasodilation of the skin with a superficial erythema, but also brings about a deep hyperaemia of the underlying tissues. It is non-irritant and can be safely used on delicate skins.

It is now being widely prescribed, with successful clinical results. Since a very small quantity is sufficient for each application, the cost of treatment is extremely low.

*Therapeutische Umschau 1952, 8, 143.

| | |
|---|---|
| *Tetrahydrofurfuryl salicylate* ..... | 14% |
| *Ethyl nicotinate* ..... | 2% |
| *n-Hexyl nicotinate* ..... | 2% |
| *Ethyl p-aminobenzoate* ..... | 2% |
| *Water-miscible cream base ad* ..... | 100% |

*"Thank you, doctor"*

Transvasin is available in 1 oz. tubes, basic N.H.S. price in the U.K. 2/6 plus P.T., and is not advertised to the public. It may be prescribed on Form E.C.10. Samples and literature will be gladly sent on application.

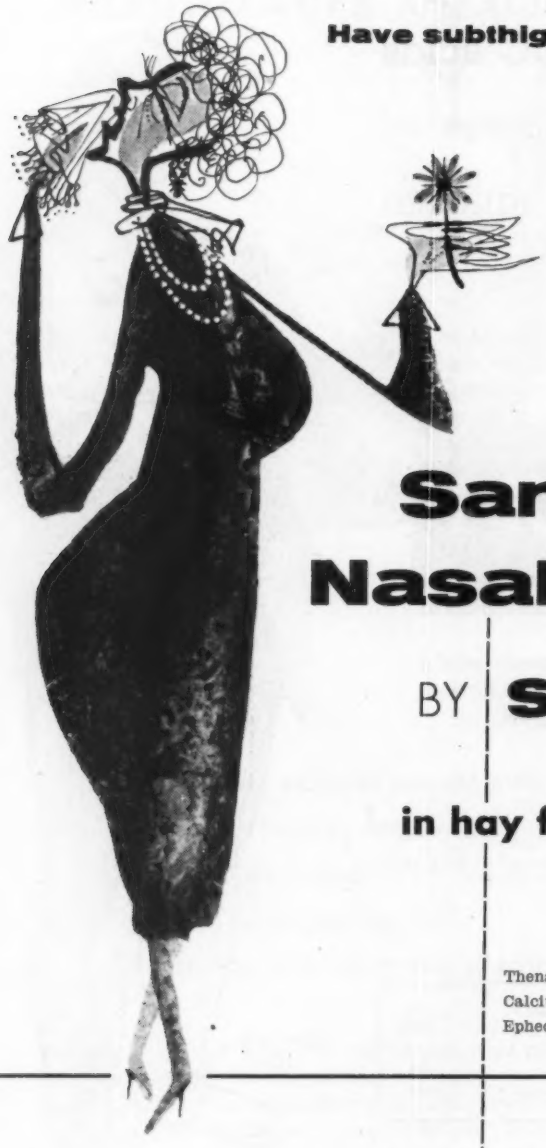
# LLOYD-HAMOL LTD

11 WATERLOO PLACE, LONDON, S.W.1. WHITEHALL 8654/5/6

*Transvasin is the registered trade mark of Lloyd-Hamol Ltd.*

♪ The flowers that bloob id the Sprig, tra-la,

Have subthig to do with the case ♪



# Sandosten Nasal Spray

BY **SANDOZ**

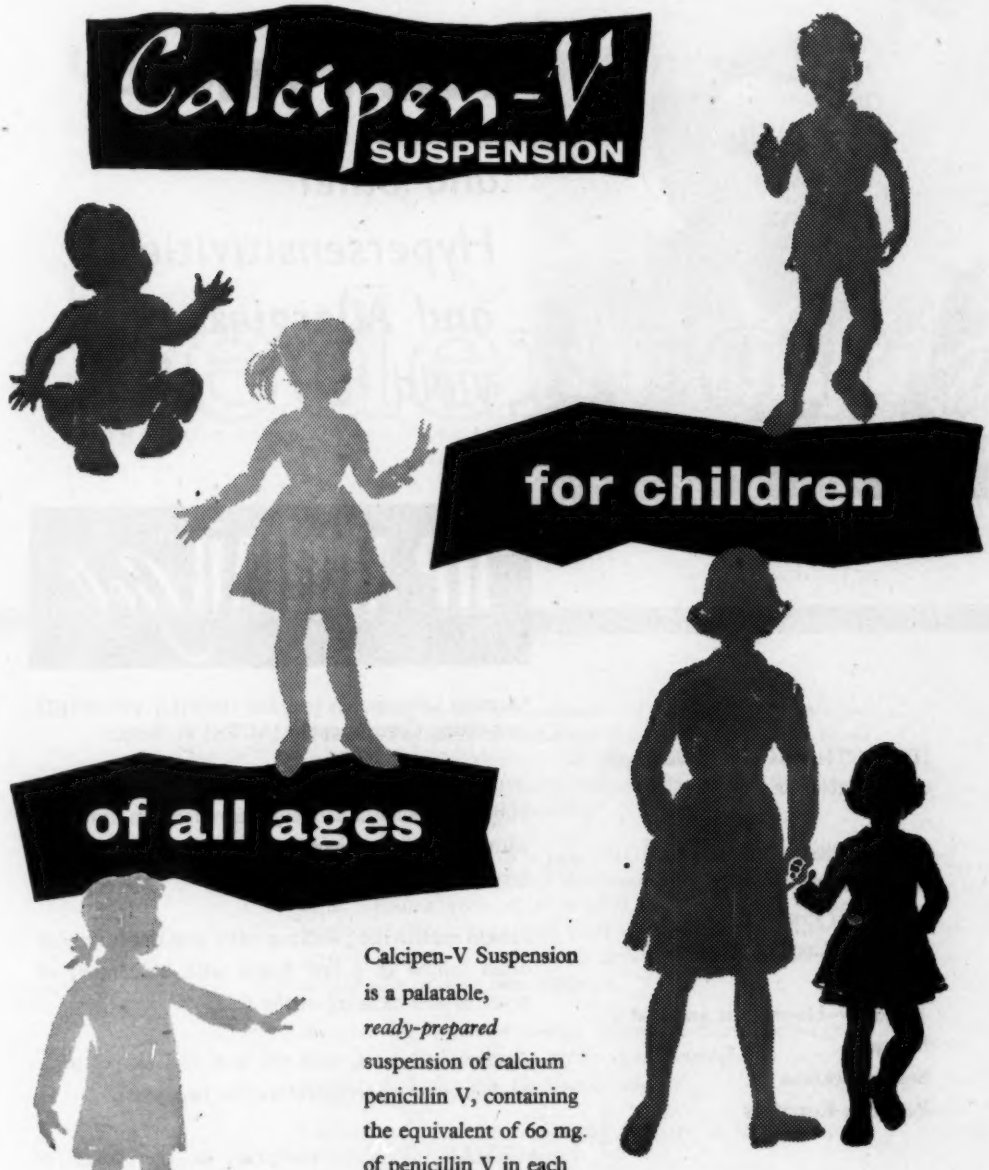
**in hay fever**

Thenalidine digluconate 0.5% w/v
Calcium lactobionate 17.5% w/v
Ephedrine hydrochloride 0.9% w/v

**Sandoz Products Limited**

**Sandoz House**
**23 Great Castle Street**
**London, W.1**

# Calcipen-V SUSPENSION



for children

of all ages

Calcipen-V Suspension is a palatable, *ready-prepared* suspension of calcium penicillin V, containing the equivalent of 60 mg. of penicillin V in each 5 ml. It is supplied in bottles of 60 ml. Calcipen-V is also supplied as tablets containing the equivalent of 60, 125 or 250 mg. of penicillin V. Professional sample and detailed literature gladly sent on request.

BOOTS PURE DRUG CO. LTD., NOTTINGHAM, ENGLAND

Boots

# ASTHMA

*and other Hypersensitivities and Allergies yield to*

# HP ACTHAR *Gel*

*Armour Laboratories brand of HIGHLY PURIFIED long-acting Corticotrophin (ACTH) in Gelatin

HP* ACTHAR Gel provides rapid effective relief in

**Status Asthmaticus**
**Angioneurotic Oedema**
**Anogenital Pruritus**
**Drug and Contact Dermatitis**
**Hay Fever**
**Jaundice—Haemolytic acquired**
**Urticaria**
**Serum Sickness**
**Penicillin Reactions**

**Available to Hospitals only**

Subjective relief in bronchospasm is often dramatic with impressive objective improvement of respiratory function.

In skin sensitivities, striking relief and improvement often follow in a few hours with abatement of pruritus and clearing of the skin.

Available in 5 ml. vials (20 and 40 I.U. per ml.). Stable at room temperature for two years.

ACTHAR is also available in the form of Lyophilized Powder for Intramuscular injection in vials containing 10 and 25 I.U. per vial, and for Intravenous injection in vials containing 30 and 75 I.U. per vial.

***Fully documented literature will be gladly supplied on request.***

**THE ARMOUR LABORATORIES**
(Armour & Company Ltd.) Hampden Park, Eastbourne, England
*Telephone: Hampden Park 740* *Telegrams: 'Armolab' Eastbourne*

# Lederle proudly announces the introduction of

# Ledercort*

TRIAMCINOLONE (9 ALPHA-FLUORO-16 ALPHA-HYDROXYPREDNISOLONE)

## a new, superior corticosteroid of great promise

LEDERCORT is an achievement of Lederle corticosteroid research—created to minimise the major deterrents to all previous steroid therapy. It offers increased potency for greater clinical effectiveness; reduced dosage and the distinct advantage of fewer side effects.

LEDERCORT represents a new HIGH in anti-inflammatory effects with a lower dosage that averages ⅓ less than prednisone. LEDERCORT offers a new LOW in the collateral hormonal effects associated with all previous corticosteroids since it causes: *no oedema, no hypertension, no psychosis, no weight gain or potassium depletion.*

Because of its reduced dosage, there is a lower incidence of other side effects such as *peptic ulcer, osteoporosis, epigastric distress, diabetic state, Cushinoid "obesity".*

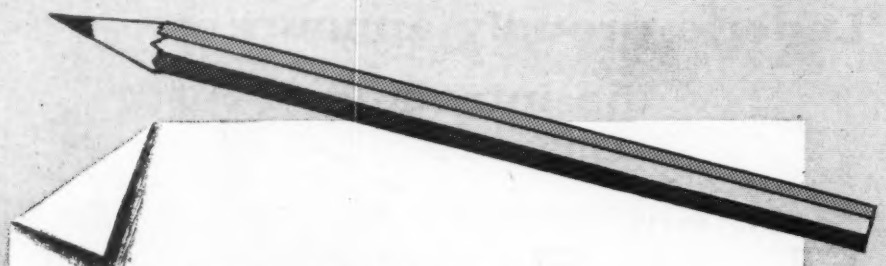
LEDERCORT provides prolonged therapy at less cost with easier patient management.

**INDICATIONS:** *Rheumatoid arthritis; bronchial asthma; dermatoses; allergic disorders; other conditions where corticosteroids have proved beneficial.*

Oral tablets of 4 mg., scored for easy division.
Bottles of 30, and 100.

*REGD. TRADEMARK

Lederle LEDERLE LABORATORIES DIVISION
Cyanamid OF GREAT BRITAIN LTD., London, W.C.2



Interim report on

# PLAQUENIL

in Rheumatoid Arthritis

The evaluation of any drug for the treatment of a chronic disease, such as rheumatoid arthritis, is a long process and it will probably be some time before any conclusive results from the British trials at present in progress with Plaquenil are available. However, the promising results of preliminary trials with Plaquenil, and its better tolerance than chloroquine in the treatment of discoid lupus erythematosus, have already aroused considerable interest among clinicians who are treating patients with rheumatoid arthritis.

For the benefit of these clinicians we are now able to say that, when persistent side-effects are encountered during treatment with chloroquine, the substitution of Plaquenil will, in the majority of cases, be followed by the resolution of side-effects, so that therapy may be continued.

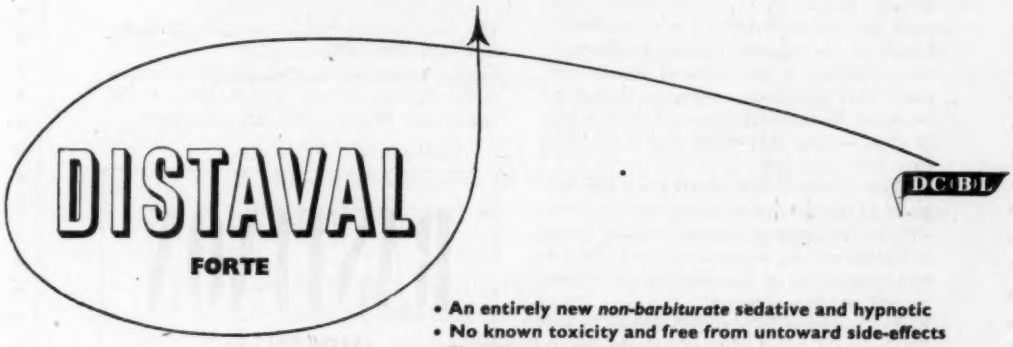
Plaquenil is hydroxychloroquine sulphate. Tablets 400 mg. available in bottles of 100 and 500.

**Pharmacological studies have shown that Plaquenil has an LD50 of 3100 ± 220 mg./kg. in mice when given orally (compared to the oral LD50 of chloroquine phosphate, which is 620 ± 80 mg./kg.)**

BAYER

**Bayer Products Limited**
Kingston-on-Thames, Surrey
Associated exporting company: Winthrop Products Limited

# safe sedation and sounder sleep




- **An entirely new *non-barbiturate* sedative and hypnotic**
- **No known toxicity and free from untoward side-effects**
- **Tasteless**
- **Calms without euphoria or initial excitement**
- **Particularly suitable for children and the aged**

**DISTAVAL**
*Scored tablets of 25 mg.*
Basic Cost to N.H.S. of 12 tablets from dispensing pack of 100 (including Purchase Tax)—1s. 3½d.
*Tube of 24 and Bottles of 100 and 500.*

**DISTAVAL**
**Forte**
*Scored tablets of 100 mg.*
Basic Cost to N.H.S. of 12 tablets from dispensing pack of 100 (including Purchase Tax)—3s. 5½d.
*Tube of 12 and Bottle of 100.*

**FOR SEDATION:**
*Adults:* One 25 mg. tablet 2 or 3 times a day
*Infants and Children:* Half to one 25 mg. tablet, according to age, 1 to 3 times a day

**AS A HYPNOTIC:**
One 100 mg. tablet 20 minutes before retiring

**THE DISTILLERS COMPANY (Biochemicals) LIMITED**
BROADWAY HOUSE, THE BROADWAY, WIMBLEDON, LONDON S.W.19
Telephone: Liberty 6600
*Owners of the trademark DISTAVAL*

PPH 1 58

# *Treatment of*

# DIABETES MELLITUS

## *without injections*

Rastinon »Hoechst« tablets provide an oral treatment for certain diabetic patients.

**EFFECTIVE** A number of patients on small regular doses of insulin have been found to be suitable for treatment with Rastinon »Hoechst« tablets. Clinical work throughout the world has shown that approximately a quarter of all diabetics can be stabilized on Rastinon »Hoechst« tablets. A few of the more recent references to the literature are given opposite.

**SAFE** The selection and stabilization of diabetic patients should be carried out under strict medical supervision. For those patients found to be suitable, Rastinon »Hoechst« tablets provide a safe form of therapy and many have now been on oral treatment for two years. No cases of proven dyshaemopoiesis or other serious side-effects due to the drug have been reported.

**SIMPLE** From 2 to 4 tablets a day are normally all that is required to replace the insulin with its concomitant syringe, needles, swabs, and often nursing assistance as well. The normal regime of urine examination and dietary control remains necessary.

**Packs:** bottles of 100 and 500 tablets.

The basic price to the National Health Service as dispensed from a 500 tablet bottle is 2.97d per tablet and the total cost to the National Health Service, with all allowances, is less than 4d per tablet.

Each tablet contains 0.5 G. of N-Butyl-N'-toluene-p-sulphonylurea; (Tolbutamide).

**REFERENCES:**


Oral Therapy for Diabetics with Tuberculosis, *Brit. Med. J.*, 1958, **1**, 220

Oral Treatment of Diabetes with Tolbutamide, *Brit. Med. J.*, 1957, **2**, 1345

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Editorial—Tolbutamide in Diabetes, *Brit. Med. J.*, 1957, **2**, 343

Oral Hypoglycaemic Compound, *Brit. Med. J.*, 1957, **2**, 352

The Antidiabetic Sulphonamides, *J. Endocrinology*, 1957, **15**, 45

Clinical Studies of the Hypoglycaemic Action of the Sulphonylureas, *Lancet*, 1957, **1**, 753

*Dtsch. med. Wschr.*, 1957, **82**, 1513-1592


# RASTINON

**»HOECHST«**

**TABLETS**

(TOLBUTAMIDE)

**HOECHST PHARMACEUTICALS LIMITED · SLOUGH**

*Distributors in the United Kingdom*

HORLICKS LIMITED · SLOUGH · BUCKS

# 'Marsilid'

TRADE MARK BRAND

## IPRONIAZID

'Marsilid' is a potent amine oxidase inhibitor and, as a consequence, intervenes in the metabolism of amines such as serotonin, adrenaline and noradrenaline. It is probable that this property of 'Marsilid' accounts for many of the observed clinical effects of this drug.

The clinical uses of 'Marsilid' include:

DEPRESSIVE STATES

The typical reaction to isoniazid consisted of a feeling of well-being, accompanied by improved appetite, increased energy and diminution of sleep requirements.

*J. nerv. ment. Dis., 1956, 124, 322.*

ANGINA PECTORIS

In man, the administration of iproniazid resolves the syndrome of angina, relieving pain and increasing the capacity for effort.

*Arch. Inst. Cardiol. (Mexico), 1957, 27, 563.*

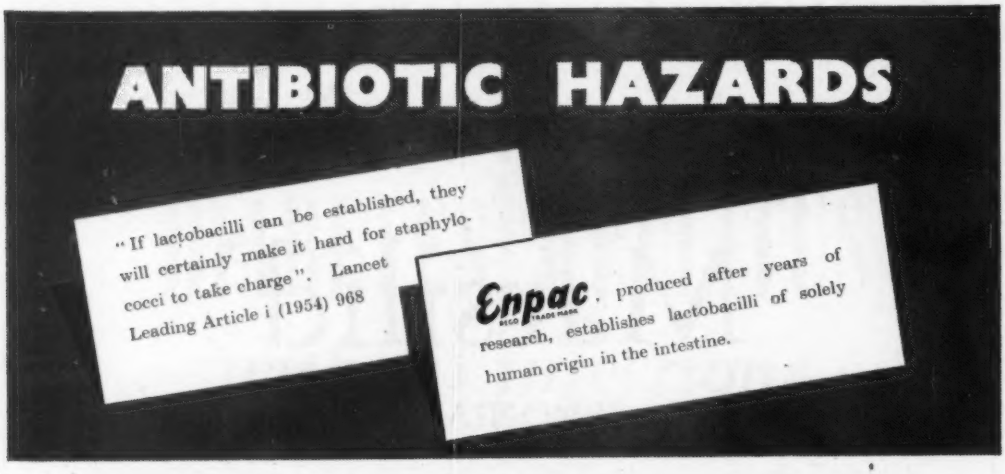
RHEUMATOID ARTHRITIS

The favourable effects of the hydrazides, especially iproniazid, on subjective manifestations in patients with rheumatoid arthritis were the most interesting and perhaps the most significant findings of this study.

*Cleveland Clin. Quart., 1957, 24, 90.*

*Marsilid Tablets 50 mg. in packings of 100.*

ROCHE PRODUCTS LIMITED, 15 MANCHESTER SQUARE, LONDON, W.1


ANTIBIOTIC HAZARDS
"If lactobacilli can be established, they will certainly make it hard for staphylococci to take charge". Lancet Leading Article i (1954) 968
Enpac, produced after years of research, establishes lactobacilli of solely human origin in the intestine.

## Restoring the balanced gut flora

ENPAC is a new and unique preparation of antibiotic-resistant strains of Lactobacillus acidophilus in a vehicle of the vital growth factors necessary for the strains to become established and multiply in the human gut. When administered during oral antibiotic therapy, these strains replace the intestinal strains of L. acidophilus, and an important part of the bacterial flora is maintained intact. There is substantial evidence which has proved that ENPAC can also be highly beneficial in certain intestinal disorders.

*Extract from* Lancet *article on clinical trials at Bristol* :

"It was found that the staphylococci increased in both groups at the beginning of antibiotic therapy. Staphylococci continued to increase in the patients taking the antibiotic alone, but in those taking Enpac there was a pronounced drop in numbers following the initial rise. Simultaneously, in this latter group the lactobacilli were rapidly established and continued to multiply. This followed the elimination of the normally non-resistant lactobacilli by the antibiotic during the early days of treatment." (*Lancet*, 1957, i, 899)

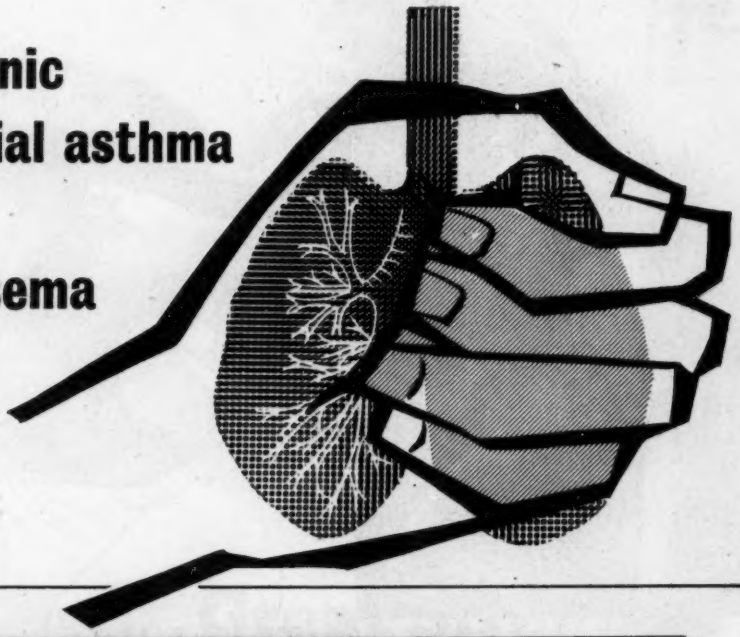
**Enpac**

ENPAC is prescribable on Form E.C.10. Basic N.H.S. Price 14/5 per 60 gramme tin.

*Samples and literature will be sent to the medical profession on request.*

**Developed by Aplin & Barrett, Ltd., Biologicals Division.**
**Distributed by : LLOYD - HAMOL LTD.**
**11, Waterloo Place, London, S.W.1. WHItehall 8654/5/6**

# In chronic bronchial asthma and emphysema



## CHOLEDYL*

| before CHOLEDYL | | after CHOLEDYL |
|---|---|---|
| | *reduces the need for aerosol therapy* | |
| | *reduces coughing* | |
| | *increases vital breathing capacity* | |

- provides a degree of effectiveness that cannot be obtained from aminophylline
- increases cardiac output
- stimulates the respiratory centre
- prevents bronchospasm without central nervous stimulation
- helps relieve the interstitial œdema
- is well tolerated
- maintains efficacy during prolonged administration

**STANDARD REFERENCE CARD ON APPLICATION**

Choledyl is available in tablets containing 100 mg. and 200 mg. choline theophyllinate and is supplied in bottles of 100 and 500 tablets.

*Manufactured in England by* ALLEN & HANBURYS LTD LONDON E2

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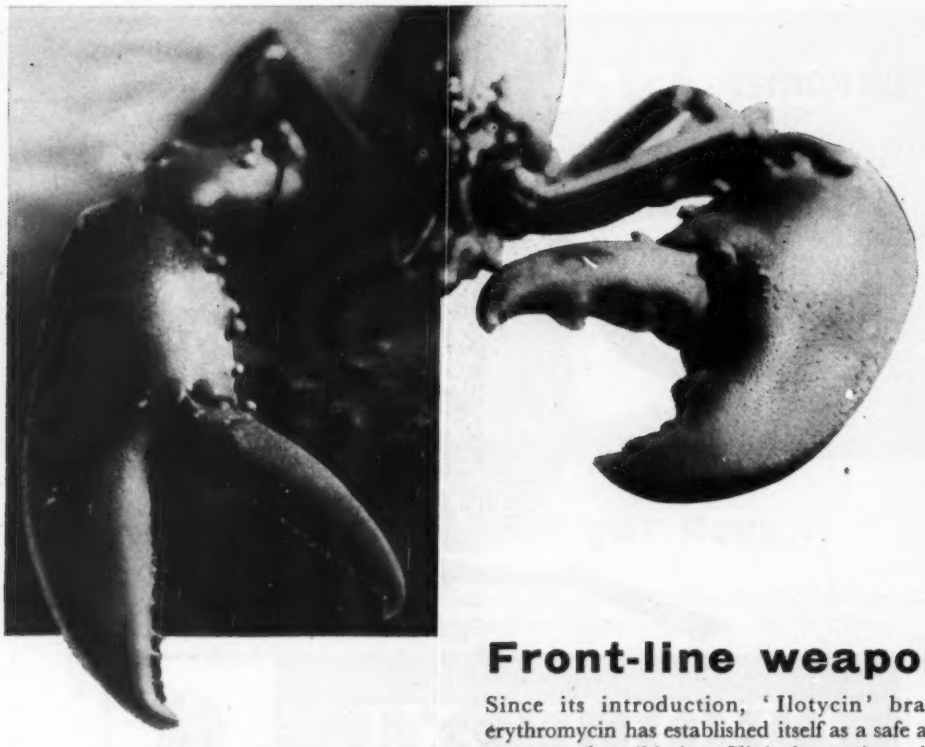

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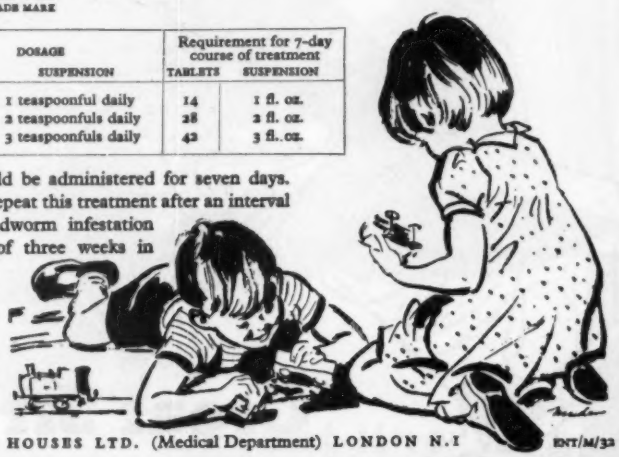

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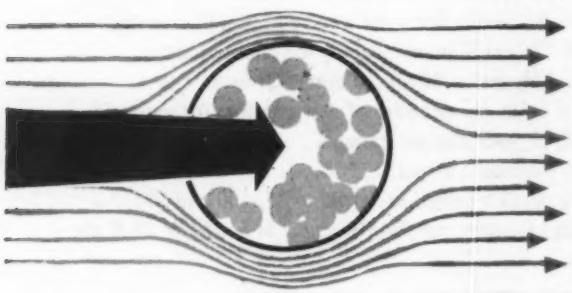

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# ADMINISTRATIVE THERAPY
## ITS CLINICAL IMPORTANCE IN THE MENTAL HOSPITAL *

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PSYCHIATRY today is becoming steadily more specialised, and the day of the old-time medical superintendent who was master of all possible trades within the asylum has passed. He was at once senior psychiatrist, consultant physician, medicolegal expert, morbid pathologist, and general practitioner to the resident staff. Today no-one is called upon to exercise all these skills, and there is a chance to examine afresh the work and role of the medical superintendent and see what therapeutic possibilities they offer. From my attempt to study this I have emerged with a concept of Administrative Therapy—the art (perhaps some day to be a science) of treating psychiatric patients in a mental hospital by administrative action. Group therapy developed from individual therapy; administrative therapy is treatment of a much larger group, the hospital. It draws on the knowledge and skills of psychiatry and group psychotherapy, the experience of the professional administrators, and the accumulating contributions of the social anthropologists.

### The Administrative Role

What does the role of medical superintendent mean to the doctor who undertakes it? What limitations and obligations does it place on him? Every psychiatrist cherishes a fantasy of what he would do if he were medical superintendent of his hospital; the essence of this fantasy is the delusion that the medical superintendent is omnipotent and can do anything he wishes. A doctor who becomes medical superintendent soon finds out how limited he is; there are so many things that he cannot do or that take a long, long time. There are the obvious limitations which block his programme—shortage of money, ancient buildings, overcrowded wards, shortage of nurses, not enough doctors, conservatism of those long in office, limitations of Treasury finance, and the tremendous difficulty (in the complex organisation of the National Health Service) of getting any new idea accepted. All these things are well known and understood. Underlying them all is the inertia of any large human organisation, which is the sum of the unwillingness of many people to change their ways.

More limiting than the things he cannot do, however, are the things he must do. Every administrator must carry out a number of ritual public actions which can be performed by no-one else; they may be disturbing, frustrating, or merely boring, but he must do them. It is in this context that the word "role" which we use so glibly approximates most closely to its theatrical meaning, for the leader of any organisation has to perform certain acts which are prescribed for him and for which he may personally have little taste. He is the figurehead, the spokesman, and at times the voice of conscience; these duties take up time which he often feels to be wasted, for they give him no feeling of achievement and certainly none of "proper work".

As figurehead he must function on public occasions, making speeches, setting forth the principles of the organisation, proposing votes of thanks graciously; he must offer public congratulations; he must make presentations to the employees who have been a long time in the hospital; he must speak at nurses' days and at the opening of new buildings. At all these times he must express the feelings of the staff and the patients and yet at the same time draw out unifying themes and suggest future goals. He must act as chairman of certain essential coordinating committees within the hospital, where departments are in conflict and only he can mediate. It is only reasonable to hand over some of these tasks to others, but he must beware how often he does this; he must remember that there is always a loss of definition when he does.

There are aspects of the role which may be frankly repugnant, especially to a sensitive psychotherapist. Promotion must be made; every time one person is gratified by promotion several are dissatisfied or even embittered. When someone breaks the rules, the administrator must not shirk the unpleasant duty of seeing the errant offender, cautioning him, and if necessary discharging him. Much can be done to obviate social disturbance by fair dealing, by constant self-scrutiny, and by willingness to admit mistakes; but there comes a time when someone must pronounce the community disapproval of an individual's actions, and the leader of the community forfeits its confidence and weakens it if he is not prepared to do this.

The administrator should not actively seek transgressors; seeking transgressors is an antitherapeutic activity best left to those whose task it is, such as auditors. If communications are free, malpractices soon come to light; if an irregular procedure gives no-one cause for complaint, then there is little need to seek it out. If an administrator spends his time checking his juniors, he conforms to the traditional asylum stereotype of fault-finding authority and soon paralyses the hospital. His task is the more difficult one of seeking out and encouraging initiative and therapeutic development.

The doctor who becomes medical superintendent will learn some of the lessons and pains of administration. He will find folklore and fantasy condensing about him whatever he does, so that he will be credited by some with magical prescience and wisdom, and by others with malignant cruelty and foolishness. He will find injustice and even tyranny exacted in his name. He will learn the gratification of seeing a change, long fought for, produce the desired result, and the bitterness of espousing and effecting a change only to see it fail because of flaws he had not perceived. He will learn how long it takes to bring about a change; how change imposed is of little value; how patience and a sense of timing often achieve more than enthusiasm.

The role of medical superintendent, like every other worth-while role in life, will have a moulding effect on him. To the characteristics developed by years of medical responsibility will be added characteristics of the wielder of power—the cautious utterance, the guarded promise, the ready excuse that saves the need of self-scrutiny, the specious justification, the growing pomposity and intolerance of criticism, the diminution of scientific detachment. All these will come, and his friends and colleagues will commiserate with his wife as they become more obvious.

### Medical or Lay?

These are some of the experiences and problems that face any administrator. Is a doctor, a psychiatrist, the person to undertake them? Administration of general hospitals is carried out by non-medical professionals in England (though not in Scotland); some of them have

* Based on an address to the psychotherapy and social-psychiatry section of the Royal Medico-Psychological Association on Oct. 9, 1957.

pressed strongly that the mental hospitals would also be better out of the hands of the doctors—though they state this as an altruistic desire to "free the doctors for their proper work". The debate often reaches a high pitch of acrimony as the well-organised and vocal groups battle for privilege and power; many of the arguments are specious, transparently self-interested, and valueless except as debating points. But the question must be considered. A bad administrator is a disaster for any hospital, be he medical or lay—and examples of both are easy to find in English hospitals. Their faults are different but equally pernicious. The bad lay administrator is a petty-minded bureaucrat, ruled by regulations, frightened of responsibility, and insensitive to human needs; the bad medical administrator is a patient-centred doctor who regards administration with contempt, who lacks the ability to plan and think ahead, the courage to face group situations, and the imagination to understand the problems of non-medical professional groups.

Any doctor who undertakes to be an administrator must accept what that means. He must be prepared to learn something of administration; he must have an interest and ability in handling, leading, and uniting people. He must be tolerant of the status systems of professions other than his own, and understand that coming in by the front door, or wearing a collar, may mean as much to someone as the right to a long white coat once did to him. He must learn a smattering of many jargons. He must lend an interested ear to the catering officer, the engineer, and the garden manager, and must understand what pains them. He must, too, be ready to think seriously about the structure of authority and organisation; it is not enough to rely on traditional modes of direction.

Doctors do not generally make very good administrators. All their training has been away from this, and if a doctor is a good administrator it is because a talent for handling groups and an interest in working with them has survived his medical training. Throughout the medical training, skill is developed towards a two-person situation, and a very special two-person situation—the handling of a patient who is often socially and intellectually inferior to the doctor, and, if he is not, is unmanned by anxiety, pain, and fear of death. The doctor is the expert whose words are weighty and powerful; his verdict is the utterance of a judge. The psychiatrist and the psychotherapist are further trained to think of the individual patient and his good, but seldom of the good of the community or the group.

The doctor with experience of group or social therapy comes to administration with an advantage. He has learnt to think in terms of the group rather than the individual; he has already begun to swing away from the exclusive one-patient orientation of the traditional doctor and traditional psychotherapist. This is of great value when he comes to administration, where every decision has to take into account the needs of a number of individuals. In his group therapy he has acquired an ability to handle the group situation, which again is valuable. Many medical superintendents never acquire this: when they are alone with a patient or with a junior doctor they are competent and powerful; when faced by a group they become anxious, secretive, and fear-ridden. A group therapist, however, should have worked through this. He can sit among a dozen other people, watch what they are doing, listen to what they are saying, and contain the anxiety that arises in him when heavy hostility or pressure is directed against him; he can feel what is happening, engage in the interaction, and yet keep sufficiently apart to observe it and wait his time for joining in.

The psychiatric administrator has to take part in one group which is an entirely new experience to him—the management committee. Here he is not the leader, the therapist doctor, the omnipotent expert; he is not even a member of the committee, he has no power to vote, he is merely an official. The determination of policy is in the hands of the committee.

This role comes hard to doctors, for they are accustomed to being experts, and the experience of working with lay committees can be peculiarly disturbing for them. Perhaps for the first time since he entered medical school the doctor meets laity who may not be much impressed by his statements and can say so; who do not credit him with omniscience. Those fascinating and admirable people who give constant and assiduous voluntary service on committees have limited respect for experts of any kind, including doctors. They themselves are magistrates, town councillors, and aldermen; accustomed to judge the affairs of their fellow men and make decisions affecting the lives of others. They have often heard experts explain with specious technical jargon why certain courses must be followed, and they are no longer to be taken in. They have seen through borough surveyors, have deflated headmasters, and have goaded medical officers of health into action; they are little impressed by oracular certainties. If the medical superintendent wishes to carry the management committee with him he must learn to justify his policies on sound well-based grounds of the general good. They will allow the doctor his full meed of expert knowledge but if he wishes to spend more public money, he must show good reason why.

### The Fabric of Human Relations

The third report of the World Health Organisation's Expert Committee on Mental Health[1] said that the most important single factor in the efficacy of the treatment given in a mental hospital is "an intangible element which can only be described as its atmosphere". They gave in detail some of the elements which make up that atmosphere, and went on to say:

> "As in the community at large, one of the most characteristic aspects of the psychiatric hospital is the type of relationship between people that are to be found within it; the nature of the relationships between the Medical Director and his staff will be reflected in the relationships between the psychiatric staff and the nurses and finally in the relationship not only between the nurses and the patients but between the patients themselves."

This is a challenging statement, and contains the kernel of administrative therapy—which may be defined as the manipulation, modification, and constant scrutiny of the relationships spreading out from the administrator, with the aim of controlling their effect on the patients.

Administrative therapy is in much the same state as psychotherapy was in the 1880s. At that time many doctors, neurologists, and alienists were talking to patients about their lives and their problems and helping them; some were exhorting patients to follow different modes of behaviour and by that exhortation were improving their adjustment to life. There was, however, no awareness of what they were doing, no insight into the factors concerned, and such instructions as they gave were based on

1. World Health Organisation. Third report of the Expert Committee on Mental Health. Geneva, 1953.

self-evident principles. Then Freud showed how much more went on between the doctor and the patient, and interpersonal reactions began to be explored. After fifty years we are now at last beginning to understand something of the dynamics of the two-person therapeutic situation. Administrators at present tend to handle their organisations with as much insight as Charcot used with his hysterics; they proceed from intuition, self-evident deductions, and political theory, their only guide being catchwords and slogans. We need to study how actions and activities of the administrators finally affect the patients, and (more important) learn how to alter these actions therapeutically. In this way we shall develop some knowledge of administrative therapy.

The fathers of institutional psychiatry had no doubt in their minds about the importance of administrative therapy though they called it " moral management ". One has only to read Tuke's *Description of the Retreat* [2] or Pinel's *Treatise on Insanity* [3] to see the importance they give to the management of the house; both stressed how unimportant formal medicine is and how useless drugs, bleeding, and purgation. Both of them discussed with admiration the work of the men who ran their hospitals; Pinel rapturised about Pussin, Tuke soberly praised the skill and consideration of Jepson; both devoted large sections in their books to describing just how the asylum should be organised and the rules that should be laid down for the life of the patients.

In each generation reformers arose, like Kirkbride in America and Simon in Germany, who restated some of the principles, occasionally with an individual twist of their own; they were heard for a time, and then they were forgotten and dropped away. The W.H.O. report sets out the principles yet again, and they are very similar to those of Tuke and Pinel. Patients are to be trusted and given as much freedom and responsibility as possible; their individualities must be preserved, and the life in hospital made as much like that outside as possible, particularly by providing regular planned and sustained activity and employment.

## Four Principles

When a psychiatrist decides to become a medical superintendent how can he look at his job? What are the principles that he is to follow? There are four main facets of administrative therapy:

1. Organisation of the patient's life
2. Staff organisation
3. Medical organisation
4. Community leadership

These are, of course, interlinked, and maladroitness in one affects the others; but they are in some degree separate. Of every action one must ask the dynamic questions: How was it done? Did it have the effect desired? What other side-effects did it have? Did it help the patients?

### *Patient's Life*

The first is perhaps the easiest of the four, for a great deal is known about it. The ideas of moral treatment and the principles put forward by the W.H.O. report give a start. It would take several years' work in any hospital to get these accepted as a fundamental way of life. The abolition of restraint, seclusion, locked doors, and over-sedation is the first move. Proper segregation into wards each with a definite function is of great value. Diligent organisation of a full work therapy programme for all patients in the hospital takes time and it must include a proper system of rewards and payments. These first essentials can be fairly easily achieved over a few years, though a close guard must be kept against the custodialism which is forever creeping back under the guise of economy and " efficiency ". Next comes the development of self-government for the patients and experiments in communal living—group therapy, discussion groups, play-reading, hospital magazines, and mixed units.

### *Staff Organisation*

To organise a therapeutic staff is more difficult. The staff in any mental hospital has been trained for years in custodial attitudes; they were trained to count patients and to watch stock, they learnt that an escape was the most awful sin—worse even than a suicide or an accident—and they have acquired whole series of custodial and often punitive reflexes that are not easily abandoned. In most hospitals, too, there is a rigid hierarchial system with orders passed down from above and a severe blockage on the flow of information upwards; there are usually rigid status barriers between the different categories of staff. The administrative therapist must decide what to tackle first. He cannot just plunge in naïvely with the ideas of making everybody democratic; if he endangers the security of senior staff, he himself may be extruded.

The emphasis should be first on communication. Meetings should be held with various groups of staff and they should be encouraged to bring forward ideas; through such meetings new channels of communication can be laid down. It is a grave mistake to come to the conclusion that some person or other is nothing but a bar to all progress and to attempt to " drive him out ". If your patients are to have human dignity, your staff must have it too. The only correct assumption is that everyone has something to contribute and that given the chance he will do his best.

Questions of responsibility and authority are central and must be constantly studied. In most mental hospitals there is scope for far wider devolution of responsibility.

### *Medical Organisation*

The administrative therapist must give special thought to the organisation of the doctors. They may have little interest in his abilities as a social therapist, but they wish to believe that he can practise their art of clinical psychiatry at least moderately well. The medical superintendent should continue to see his own cases and have cases within the wards, otherwise he will no longer understand his colleagues' problems. The relations of the administrative therapist with the consultant psychiatrists are a difficult and testing point. At present there is much pain and bitterness about this in English mental hospitals. Some medical superintendents still think in terms of the pre-1948 situation, when the medical superintendent was personally responsible for the treatment of every patient. Today the consultant psychiatrist has full responsibility before the Law and before society for the treatment of his patients, and there can be no excuse for the medical superintendent interfering in the treatment prescribed. But the issue goes deeper. The consultant psychiatrists are the only group of peers whom the medical superintendent meets; the only group who share his professional training. Many consultant psychiatrists despise administration and do not think much of administrative therapy or social psychiatry. What they want to do is to treat individual patients in the one-doctor/one-patient relationship; this they think of as the highest good. The administrative therapist's task is to provide a milieu in which everyone may do his chosen job to the best of his ability without interference, and this is as true of the consultant psychiatrist as of humbler people in the organisation. If an administrative therapist does his own job well and takes the same care to avoid trespassing on another doctor's patients that is standard throughout medicine, his relations with his consultant staff should be good. If he can provide them with the facilities they need to do their work, free of the more vexatious hospital irritations, he will gain their gratitude and respect.

2. Tuke, S. A Description of the Retreat. York, 1813.
3. Pinel, P. A Treatise on Insanity. London, 1806.

The medical organisation will vary with the size of the hospital. It has been suggested that the best size of unit for administrative therapy is about 300 beds; it is still just possible to administer 1000 beds as a unit. With larger hospitals, however, the span becomes too great and it is necessary to split the hospital into "firms" running self-contained units with a consultant and senior nursing officer in charge. The only difficulty with this is that differing cultures develop in the self-contained units; if they differ too much, it is hard for patients and junior nurses to understand that one institution can have such different units within it, and they may find the passage awkward from a liberal environment to a restrictive one.

*Community Leadership*

If any human organisation is to work well, it should have confidence in itself, it should have a policy, and it should have good morale. The administrative therapist must give these to the hospital as best he can. The hospital policy must be clearly formulated. In the past the cries have been "non-restraint" and "full activity"; recently it has been "open doors". The policies of the W.H.O. report must be worked into the structure of the hospital and embodied in slogans which can be understood by the most uninterested staff member. They must be repeated again and again until they really have meaning and until the words "therapeutic community" mean not just the bee in the superintendent's bonnet but a way of living and acting.

Relations upward are always difficult, and it is in this sphere that some social therapists fail sadly, while some autocratic medical superintendents have often been quite successful. The hospital management committee decide the policy of the hospital; if an administrative therapist is going to change the whole life and way of a hospital he must carry the management committee with him. They are mature and tend to conservatism; they are dubious about the enthusiasms of youth and many have much previous experience of the hospital. They must be won to new policies which must be put to them in terms of the humanitarian gain to the patient, for in this they are always interested. Beyond them the policy must be carried to the public; it is no use opening your doors if the local public and the police shout to have them locked again. In this the cooperation of the local press is vital and the administrative therapist must work with them. Cheerful reports about the hospital will dispel criticism, will build up the morale of the staff, and will do much to allay public anxieties.

**In an N.H.S. Setting**

Within the National Health Service there is constant work to do. Though new buildings do not produce good psychiatric treatment, some new equipment is needed for the hospital; and the hospital which feels that it gets the last handout of everything may become dispirited. The administrative therapist as leader of the hospital and spokesman for its policy must be prepared to argue policy up the various tiers of the National Health Service; this involves knowledge of local power relationships and a willingness to explain again and again things which seem crystal clear. It needs patience and self-control to put over an idea, which is of great personal importance, to a committee who are perhaps uninterested or committed to the needs of another hospital, and to carry conviction so that the needed money is granted.

There is also a constant defensive battle to be fought; ever busy within the fabric of the National Health Service are those white ants, the auditors, nibbling away and eroding the fabric of human relations and good feeling. They are employed to peer through every hospital attempting to prove that everyone is dishonest and that no-one can be trusted; given their way they would multiply the regulations until the hospital was bound in a cocoon of red-tape, all in the name of "efficiency". They must be watched unceasingly and every claimed advance in efficiency scrutinised with great care to see it does not harm the human relations of the hospital. Luckily they too are only servants, and the masters are the hospital management committee, the representatives of the public; if an administrative therapist is worth his salt he can carry the point against the auditors and show that the welfare of the patients and the trust and happiness of the staff are first essentials.

But the most important task of the administrative therapist is to establish the atmosphere of the hospital. And this, the most important, is the task most difficult to describe. He needs openness, consistency, respect for everyone's human dignity, and a welcome for everyone's contribution; a belief that everyone wishes to help and that no-one is past recovery—neither the most demented patient nor the most stupid nurse. For one thing is certain: as he treats his staff so will they treat the patients.

* * *

These are some of the aspects and personal meanings of the art of Administrative Therapy as they strike one new to the field, but there is so much to learn. Studies like those of Stanton and Schwartz [4] point the way to an understanding of the dynamics and the effects of administrative action. By such means, knowledge may gradually replace intuition until the art becomes a science.

## THE AUTOANTIBODY NATURE OF THE THYROIDITIS ANTIBODY AND THE ROLE OF THYROGLOBULIN IN THE REACTION

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IN rabbits, dogs, and guineapigs, intradermal injection of thyroid extract (combined with Freund adjuvants) from other animals of the same species engenders the production of organ-specific thyroid antibodies, as well as an accompanying thyroiditis (Witebsky and Rose 1956, Rose and Witebsky 1956, Witebsky et al. 1956). An extract of the animal's own thyroid gland has the same effects. Moreover, the serum of some patients with chronic non-infectious thyroiditis contains a factor that reacts with human thyroid extract, normal or goitrous (Roitt et al. 1956, Witebsky et al. 1957, Paine et al. 1957, Doniach and Roitt 1957). On the basis of the animal experiments, it has been proposed that this serum factor is a true autoantibody, and that the pathogenesis of the clinical disease is related to autoimmunisation. Additional evidence for the autoantibody nature of the serum factor is found in experiments in which thyroid extracts from numerous different individuals exhibited essentially identical titres when tested with a thyroiditis serum (Witebsky 1957). The criteria for establishing the existence of antoantibodies have been discussed by us previously (Witebsky et al. 1957).

4. Stanton, A., Schwartz, M. The Mental Hospital. London, 1955.

TABLE I—RESULTS OF TANNED-CELL HÆMAGGLUTINATION TEST

| Dilutions of Buc. serum | Tannic-acid-treated human erythrocytes (group O) coated with saline extract* of | |
|---|---|---|
| | Buc. goitre | Het. goitre |
| 1 : 20 | +++† | +++ |
| 1 : 40 | ++ | +++ |
| 1 : 80 | ++ | ++ |
| 1 : 160 | ++ | ++ |
| 1 : 320 | ++ | ++ |
| 1 : 640 | + | + |
| 1 : 1280 | + | − |
| 1 : 2560 | − | − |
| control‡ | − | − |

* Each extract diluted 1 : 100 and immersed in boiling water for 2 minutes.
† +++ to + indicates various degrees of agglutination of erythrocytes after tubes were allowed to stand overnight at 4°C.
‡ Tanned but uncoated cells. Other controls using normal human sera rather than patient's serum were uniformly negative.

Nevertheless, as Cruickshank et al. (1957) have emphasised, an important step in establishing the presence of a true autoantibody (rather than an isoantibody) is the demonstration of a reaction with the patient's own tissues. Mackay, Larkin, and Burnet (1957) have pointed to the failure of certain so-called autoimmune antibodies to react with antigens prepared from the individual's own tissues. We therefore report here an experiment illustrating just such an in-vitro reaction.

## Observations

A patient, Mrs. Buc., was operated on at the Buffalo General Hospital in October, 1956, when a large diffuse colloid goitre was removed. A sample of her serum taken at this time (Oct. 23, 1956), when examined by the tanned-cell hæmagglutination and precipitation methods, revealed no trace of thyroid antibodies. The surgically removed tissue was stored in the frozen state.

Taken four months later (March 15, 1957), a second sample of her serum produced a positive reaction in the tanned-cell hæmagglutination test for thyroid antibodies (titre 700) using pooled normal human thyroid extracts as antigen. Precipitation tests were negative. (A sample of her serum, taken in December, 1957, revealed a slight decrease in antibody titre—500). The possible clinical significance of the postoperative appearance of antibodies in this case has been discussed by Paine et al. (1957).

The patient's thyroid tissue obtained previously was thawed, and a saline extract was prepared by our usual technique. A similar extract was prepared from a second surgically removed non-toxic goitre (Het.), and both goitre extracts were used as antigens in a tanned-cell hæmagglutination test of a sample of Buc. serum. The results of the test are given in table I, which shows that the patient's serum agglutinated human erythrocytes coated with an extract of her own goitre as well as the goitre extract of another person, Het. The titres in each case are the same within experimental variation, and resemble those obtained in other experiments with a pool of thyroid extracts.

We conclude, therefore, that the thyroid antigen involved was actually present in the tissues of the patient, as well as in the thyroid glands of other persons.

TABLE II—ULTRACENTRIFUGAL ANALYSIS OF PATIENT'S THYROID EXTRACT AND FRACTIONS

| Fraction | Concentration (total protein) (g. per 100 ml.) | Peak | Analysis (%) | Total thyroglobulin (g. per 100 ml.) |
|---|---|---|---|---|
| Initial saline extract | 4·07 | I | 4·51 | |
| | | II | 52·4 | 2·13 |
| | | III | 1·53 | |
| | | IV+V | 41·5 | |
| P 1·60–1·70* (" thyroglobulin ") | 2·48 | I | 2·45 | |
| | | II | 94·6 | 2·23 |
| | | IV+V | 2·99 | |
| P 1·70–4·00† | 1·93 | | | |
| RP 2·50–3·00 (" thyralbumin ") | 1·16 | V | 100·0 | |

* Precipitate obtained between 1·60 and 1·70 M ammonium sulphate.
† Residual proteins after precipitation of thyroglobulin fraction.

## Discussion

Which constituent of the thyroid extract is responsible for the reaction observed? Our preceding investigations (Witebsky et al. 1955, Rose and Witebsky 1955, Shulman et al. 1955) on the organ-specific nature of thyroglobulin suggested to us that, in animals, it would play the leading role in autoimmunisation. Similarly, Roitt, Doniach, Campbell, and Hudson (1956) have regarded thyroglobulin as the important antigen in human thyroiditis. To study this point further, the Buc. extract was fractionated by addition of ammonium sulphate in the same manner as previously described for hog-thyroid extract (Shulman 1956, Shulman et al. 1957). Ultracentrifugal analysis of the initial saline extract revealed at least five sedimenting components (table II), of which one, peak II, was identified with the classical thyroglobulin on the basis of its sedimentation constant. These sedimenting components seem to be completely analogous to those observed in hog preparations (Shulman et al. 1955, Witebsky et al. 1956). The portion of thyroid extract precipitating between 1·60 and 1·70 M ammonium sulphate shows a relative enrichment in thyroglobulin content and a considerable decrease in content of peaks I, III, IV, and V. The only other ultracentrifugal component available in purified form is peak V, the thyralbumin fraction, obtained by precipitation between 2·50 and 3·00 M ammonium sulphate (Shulman et al. 1957).

TABLE III—INHIBITION OF PATIENT'S SERUM BY VARIOUS THYROID FRACTIONS

| Fractions of Buc. thyroid | Antigen dilution |
|---|---|
| Initial saline extract | 1 : 128,000 |
| P 1·60–1·70 (" thyroglobulin ") | 1 : 64,000 |
| Residual supernatant (P 1·70–4·00) | 1 : 4000 |
| P 2·50–3·00 (" thyralbumin ") | 1 : 80 |
| Norman human kidney extract | 0* |

* No inhibition with undiluted extract.

To measure the antigen content of the various thyroid fractions agglutination-inhibition tests were set up. Serial dilutions of each fraction were prepared and added to aliquots of the Buc. serum diluted to contain about four (2+) hæmagglutination doses. After an hour at room temperature tanned human red cells coated with the Buc. thyroid extract were added to each tube, and the degree of agglutination was read in the usual way.

Table III shows the highest dilution of each thyroid component capable of completely inhibiting agglutination. The initial saline extract, as well as the thyroglobulin fraction, can neutralise the reaction of Buc. serum in high dilutions and are almost equally effective. The thyralbumin fraction and the supernatant from the thyroglobulin precipitation show relatively little activity.

These findings suggest that the antigen involved in the autoimmunisation leading to thyroiditis precipitates in the thyroglobulin fraction, and that this antigen can elicit demonstrable circulating antibodies in the same individual.

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*references overleaf*

# PRE-EPIDEMIC ANTIBODY AGAINST 1957 STRAIN OF ASIATIC INFLUENZA

## IN SERUM OF OLDER PEOPLE LIVING IN THE NETHERLANDS

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AFTER a strain of Asiatic influenza (A/Asia/Singapore/1/57) had been received by us at the end of May, 1957, from Dr. C. H. Andrewes, of the National Institute of Medical Research, London, it soon became clear, using ferret antisera, that there was no cross-overlapping of surface hæmagglutinins between the egg line of this strain and the ferret-mouse-egg lines, egg lines, and egg-mouse-egg-lines of human A strains isolated in 1933–56 or a strain of swine influenza (Swine/15) isolated by Shope (1931). Similar observations were made by Meyer et al. (1957), Jensen (1957), and Dr. A. Isaacs, of the National Institute of Medical Research, London (personal communication). Later it was shown that the same holds true for the mouse-lung-adapted line of the Asiatic strain.

When, however, a few paired sera from patients who had had influenza in 1953 were tested against the Asiatic strain, one hæmagglutination-inhibiting titre of 44 was found in a serum taken during the acute phase of the disease in a patient aged 88. Next, of 12 sera from persons aged 59–84 2 from persons aged 80 and 84 showed a positive titre.

With the aid of many doctors in the Netherlands we collected in June as many sera as possible from people aged 50–100. We already had in our laboratory sera from the younger age-groups. Altogether 1256 sera were collected and stored at −20°C. Through Dr. A. M. M. Payne, chief of the Section of Endemo-Epidemic Diseases of the World Health Organisation at Geneva, other laboratories in the world were asked to collaborate in this investigation and to collect sera as soon as possible before the Asiatic influenza had spread into their country. In the Netherlands we were just in time, because the epidemic in this country started with its first focus in the middle of June.

### Methods and Materials

*Hæmagglutination-inhibition (H.I.) Test*

Sera were examined individually for H.I. antibody against the strain A/Asia/Japan/305/1957 (passage formula $egg_x$-$ferret_3$-$mouse_6$-$egg_n$) obtained from Dr. K. Jensen. In our experience this is a more sensitive strain for this purpose than the egg-line of the strain A/Asia/Singapore/1/57 (Dr. K. Jensen, personal communication).

The titres of positive sera are expressed as the reciprocal of the dilution of the serum interacting with the virus and giving 50% hæmagglutination, being finally corrected to the use of 3 agglutinating units (A.U.) of the virus. The non-specific inhibition of the sera was abolished by the use of enzymes of *Vibrio choleræ* (see Brans et al. 1953).

After the screening of the sera had been finished, all the positive specimens were re-examined on the same day by two different workers. The final H.I. titre was considered to be the arithmetical mean of the titres obtained in both tests. Usually the titres in this final control did not differ substantially from those obtained in the screening test, the only exception being a few very low titres which in the final test proved negative. Low titres were read with great care because pattern formation in low dilutions of sera not containing H.I. antibody may be incomplete.

After the investigation had been finished, the ages of most of the people aged 70–100 who showed a positive H.I. titre were checked.

*Mouse-protection (M.P.) Test*

In the M.P. test the strain A/Asia/Ned./43/57 (passage formula: $mouse_{22}$-$egg_1$-$_4$) was used. This strain is identical with A/Asia/Japan/305/57 in the cross-H.I. test. From the emulsion of infective mouse lung of the 22nd passage the strain was grown in the allantoic cavity of the chick embryo, and the egg fluid was used in the M.P. test. The advantages of this method are that constant amounts of virus can be used in the different tests, and that the virulence of the virus can be maintained more or less constant. M.L.D. of about either 50 or 5 were used according to the H.I. titre of human serum, because usually H.I. titres below 30 could only be confirmed as true antibody in the M.P. test when fluids of low virulence were used.

TABLE I—INCIDENCE OF PRE-EPIDEMIC POSITIVE H.I. TITRES IN HUMAN SERA OF DIFFERENT AGE-GROUPS AGAINST INFLUENZA STRAIN — A/JAPAN/305/57

| Age-group (yr.) | No. of sera | No. giving positive H.I. test |
|---|---|---|
| 1–9 | 11 | 0 |
| 10–19 | 30 | 0 |
| 20–29 | 72 | 0 |
| 30–39 | 85 | 1 (1·2%) |
| 40–49 | 121 | 2 (1·7%) |
| 50–59 | 163 | 2 (1·2%) |
| 60–69 | 361 | 4 (1·1%) |
| 70–79 | 280 | 14 (5·0%) |
| 80–89 | 122 | 27 (22·0%) |
| 99–100 | 11 | 2 (18·0%) |
| Total | 1256 | 52 |

We used as control sera in each experiment homologous ferret antiserum and the sera of two persons aged 24 containing antibodies against many former human A strains except the Asiatic strain. In a second experiment it was shown that neither high-titred ferret antisera against the influenza strain A/Swine/15 nor against the egg- and mouse-lines of all the main types of former human influenza-A strains protected mice against infection with the Asiatic strain. Six mice were used per dilution of serum, but in most of the experiments only the serum dilution 1 : 2 was used. Necropsy on surviving mice was done 7–10 days after inoculation, according to the number of M.L.D. used in the experiment.

*Complement-fixation (C.F.) Test with Soluble Antigen of Influenza Virus A*

This test was made according to Hoyle (1948), egg-membranes being used for preparing the antigen.

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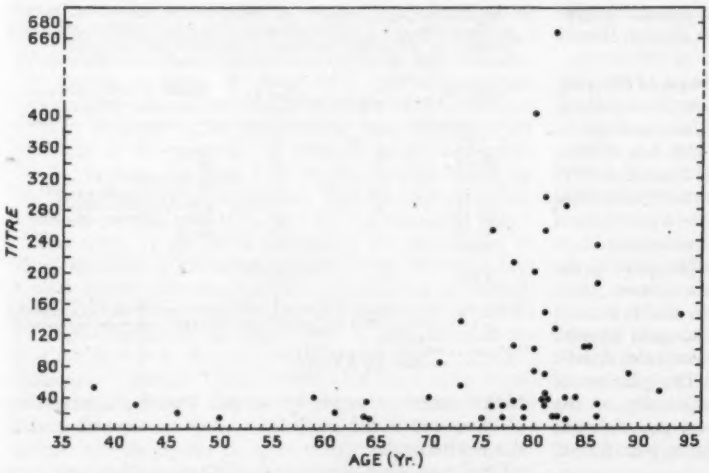


**Fig. 1—Age-distribution and positive H.I. antibody titre against influenza strain A/Asia/Japan/305/57 found in 1256 normal sera collected in Holland before July, 1957 (titres of <9 not incorporated).**

## Results

Positive H.I. titres were found in 52 of the 1256 sera examined. In the sera from persons aged 71 or more there was an increase in number of positive titres (table I and fig. 1). The total absence of positive sera in the age-group under 30 may be due to the relatively few sera available from this group. There can be no doubt that the positive H.I. titres represent true antibody, as is shown by the results obtained with the M.P. test (tables II and III). Nor can it be assumed that recent infection with the Asiatic strain type of 1957 is concerned, because of the results with the C.F. test with soluble antigen of influenza virus A. The first somewhat higher titre (87) was found in a person aged 71, and the first high titre (140) in a person aged 73. The youngest person with H.I. antibody was aged 39 (titre 54). The greatest incidence of positive titres was in persons aged 81 (8 of the 21 sera of this group showed inhibition).

Comparative titration of 49 positive sera against the Asiatic strain A/Japan/305/57, the strain A/Swine/15 and the mouse-adapted lines of 8 human A-strains from the period 1933–56 showed that in 17 sera (35%) the titre to the Asistic strain was higher than to any of the former strains (corresponding ages 76–94). In 2 sera a titre was present only to the Asiatic strain (corresponding ages 79–86). In 8 other sera the titre to the Asiatic strain was either about as high as the titre to one or more of the former strains, or amounted at least to 50% of the highest titre to one of these strains (corresponding ages 77–84). This finding is important, because it proves that in the ages 76–94 the Asiatic titres cannot in general be considered as having been caused by possibly existing shared minor antigen with known former strain types (see later). Meanwhile Davoli and Corsi (1957) have found pre-epidemic antibody to the Asiatic strain in Italian people, predominantly in the age-group 78–85.

TABLE II—M.P. TEST AND C.F. TEST WITH SOLUBLE ANTIGEN A WITH HUMAN SERA SHOWING POSITIVE H.I. TITRE AGAINST INFLUENZA STRAIN A/ASIA/JAPAN/305/57

| No. of positive H.I. human sera | Mouse-protection test | | C.F. test with soluble antigen A | | |
|---|---|---|---|---|---|
| | No. positive | No. doubtful | No. negative | No. doubtful | Serum showing own inhibition |
| 52 | 25[1] | 2[2] | 45[3] | 2[4] | 4 |

1. Complete or incomplete protection in serum dilution from 1 : 2 to 1 : 8
2. H.I. titres 13 and 20.
3. Titres from <1 : 8 to 1 : 16.
4. Dilution 1 : 32, fixation ++; and dilution 1 : 64, negative.

TABLE III—MOUSE PROTECTION TESTS

| H.I. titre | Age (yr.) | Dilution of patient's serum | | | | Dilution of Control Sera |
|---|---|---|---|---|---|---|
| | | 1 : 2 | 1 : 8 | 1 : 32 | 1 : 128 | 1 : 2 |
| 87 | 71 | ++ + 0-0 0 0 | ++++(D) ++++(D)<br>+++ ++ 0 0 | ++++(D) ++++(D)<br>++++(D) ++++(D) | ++++(D) ++++(D)<br>++++(D) ++++(D)<br>++++(D) ++++(D) | ++++(D)×11 (human)<br>0 0 0 0 0 0<br>(homologous ferret) |
| 140 | 73 | + 0 0 0 0 0 | ++++(D) +++<br>+++ ++ + | ++++(D) ++++(D)<br>++++(D) +++ ++ | ++++(D) ++++(D)<br>++++(D) ++++(D)<br>++++(D) ++++(D) | ++++(D)×10 (human)<br>0 0 0 0 0 0<br>(homologous ferret) |
| 258 | 76 | + 0 0 0 0 0 | | | | ++++(D)×10 (human)<br>0 0 0 0 0 0<br>(homologous ferret) |
| 672 | 82 | 0 0 0 0 0 0 | + + + 0 0 0 | ++++(D) ++++<br>+++ ++ ++ + | ++++(D) ++++(D)<br>++++(D) ++++(D)<br>++++(D) ++++(D) | ++++(D)×10 (human)<br>0 0 0 0 0 0<br>(homologous ferret) |
| 16 | 50 | ++++(D) + ++<br>++ ++ ++ | | | | ++++(D)×8 (human)<br>0 0 0 0 0<br>(homologous ferret) |
| 18 | 64 | ++++(D) + + ± 0 | | | | ++++(D)×8 (human)<br>0 0 0 0 0<br>(homologous ferret) |
| 16 | 86 | ++ + + + + 0 | | | | ++++(D)×9 (human)<br>++ 0 0 0 0 0<br>(homologous ferret) |
| <9 | 65 | ++++(D) ++++(D)<br>++++(D) ++++(D)<br>++++(D) | | | | ++++(D)×6 (human)<br>0 0 0 0 0 0<br>(homologous ferret) |

0–++++, degree of lung lesions (necropsy).
++++(D)×10, all 10 controls died within the period of the experiment.
(D), mouse died within the period of the experiment. Non-specific death is not recorded.

*Antibody against Current Asiatic Strain Appearing after Vaccination with Monovalent Vaccines from Former Human A Strains*

We had at our disposal 323 sera from people of different ages who had been vaccinated in 1956 and in the beginning of 1957 with monovalent vaccines of mouse-lines of former human A strains: A/PR$_8$ (1934 U.S.A.), A/FM$_1$ (1947 U.S.A.), A/1951/Scandiv. (1951 Ned.), and A/1953 (1953 Ned.).* Testing pre- and post-vaccination sera against the strain A/Asia/Japan/305/57 we found that a surprising number (9%) of the post-vaccination sera showed H.I. antibody against the Asiatic strain, even in the younger age-groups (table IV). These titres were again checked in duplicate on the same day. A few M.P. tests done with pre- and post-vaccination sera again showed increases of true antibody against the current Asiatic strain in the post-vaccination samples. The number of cases is too small to be analysed statistically in the different groups of people who received the different vaccines, but in every group increases of titre were found.

TABLE IV—POST-VACCINATION TITRES AGAINST INFLUENZA STRAIN A/ASIA/JAPAN/305/57 AFTER VACCINATION WITH FORMER HUMAN A STRAINS IN DIFFERENT AGE-GROUPS (MONOVALENT VACCINES)

| Age-group (yr.) | No. vaccinated | No. of positive H.I. titres | Height of post-vaccination H.I. titres[1] |
|---|---|---|---|
| 1–9 | 8 | 0 | .. |
| 10–19 | 14 | 2 | 18–30* |
| 20–29 | 42 | 2 | 16°–27 |
| 30–39 | 39 | 3 | 159*–23–18° |
| 40–49 | 54 | 7 | 18–38–81–87–53–14–129* |
| 50–59 | 92 | 7 | 408*–13–19–36–30–33–36 |
| 60–69 | 58 | 6 | 64–18–176*–14°–16–108* |
| 70–79 | 15 | 2 | 24–20 |
| 80–85 | 1 | 0 | .. |
| Total | 323 | 29 (9%) | .. |

1. All H.I. pre-vaccination titres of these cases were <9. Five positive pre-vaccination titres are omitted from this table and were incorporated in table I and fig. 1.
* Mouse-protection test positive.
° Mouse-protection test doubtful.

## Discussion

An outstanding finding is that the pattern of pre-epidemic Asiatic-influenza antibody in human sera shows a concentration in number and a rise in titre in people aged 71–94. Although the available number of sera in the age-group 0–30 was relatively small, it is very unlikely that, in this age-group, a similar antibody pattern would have been found as in the age-group 71 or more. This phenomenon can therefore be compared with that demonstrated by Davenport et al. (1953, 1955) and Hennessy et al. (1955) of the appearance of high-titred H.I. antibody in people aged 35–38 (in 1953) against the dominant antigen of the influenza-A strain isolated from North American swine by Shope. Fig. 2 illustrates our confirmation of this work from a few sera investigated in the Netherlands.

The first conclusion that can be drawn from fig. 1 is that the human race most probably has been in contact with the dominant hæmagglutinating antigen of the current Asiatic strain in the last quarter of the 19th century, and that the 1957 pandemic of Asiatic influenza represented, in all probability, a repetition of an epidemic from that period.

The analysis of antibody in human sera of different age-groups against the dominant antigen of the influenza-A swine strain indicates that the pandemic of 1918–19 was most probably the origin of the swine antibody in man, and that this pandemic was caused by the swine-influenza virus (Laidlaw 1935, Shope 1936, Davenport et al. 1953). It remains, however, much less certain when the Asiatic-influenza antibody pattern shown in fig. 1 originated, because most probably this figure shows only a poor remnant of a pattern which was much more extensive in number of positive titres and in height of titres shortly after the epidemic from which it was derived.

There are some indications that the antibody pattern shown in fig. 1 originated in the classic pandemic of 1889–90. The first high titres (140 and 258) against the current Asiatic antigen appear in the pattern in the ages 73 and 76, pointing to a possible origin about 1881–84. The greatest concentration of positive sera starts from the age of 76, again pointing to a possible origin around 1881. No important epidemic of influenza was registered in Europe between 1875 and 1889. Most workers (e.g., Ripperger 1892, Leichtenstern 1896), with the exception of Hirsch (1881), do not consider the epidemic of 1875 to be a true pandemic, and most probably it did not originate in central Asia.

If we assume that the pattern shown in fig. 1 originated in the pandemic of 1889–90, an explanation should be sought for the fact that, in the age-group 70–76, only 5 positive H.I. titres were found in 161 examined sera (3·1%). A

* These vaccines were kindly produced at our request by the Biological Laboratories of N. V. Philips Roxane, Weesp.

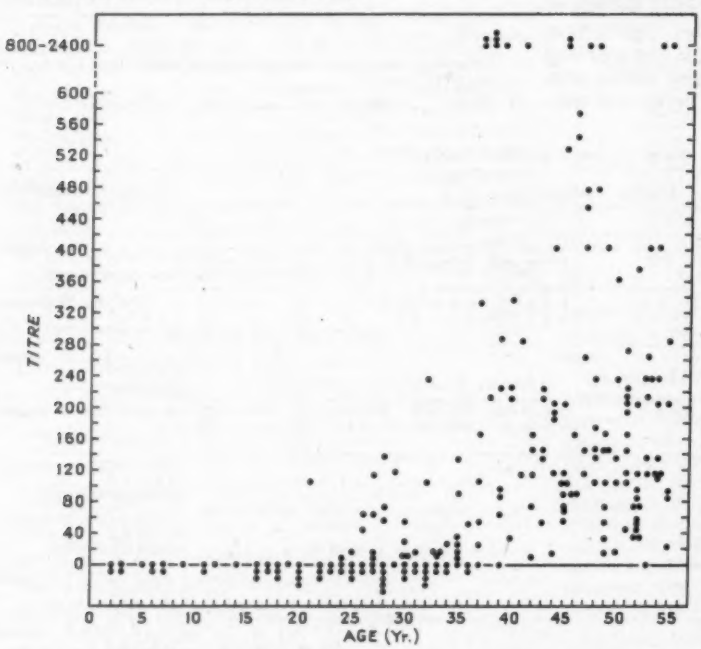


**Fig. 2—Age-distribution and H.I. antibody titres against influenza strain A/Swine/15 found in sera collected in Holland at beginning of 1957 (titres of <9 placed on or below zero line).**

possible explanation may be that in the pandemic of 1889–90 school-children perhaps had a higher incidence of disease than had younger children, as was reported by several workers at that time (*Mitteilungen des Statistischen Amtes der Stadt München* 1891, Schmid 1895). Possibly other laboratories may supply more evidence of the presence of antibody in the age-group 70–76, because we must look on the pattern shown in fig. 1 as due largely to chance. The absence of a clear antibody pattern before the age of 70 is discussed below.

The 1890 origin of the antibody pattern shown in fig. 1 can also be explained on theoretical grounds. It is almost certain that the pandemic of influenza of 1889–90 originated in central Asia. The first cases were described by Heyfelder (1889) in May, 1889, in Bokhara, and the Russian doctors at that time called the disease "Chinese" influenza. Although Cantlie (1891) described an epidemic of febrile respiratory disease in September, 1888, in Hong Kong, thought by him to have been influenza, we cannot accept this diagnosis, because of the high incidence of skin rash in these patients and the appearance of jaundice in several cases.

The epidemiology, of "true" pandemics of influenza differs sharply from that of the waves of seasonal influenza. True pandemics start in a certain part of the world, spread with the speed of human traffic irrespective of climatic and seasonal influences, and show a high morbidity, especially in people aged less than 40, and a relatively low mortality in their "first" wave.

Since the discovery of the human influenza virus (Smith et al. 1933) we know that interpandemic (seasonal) influenza virus A is continuously circulating in the world population, changing from time to time its antigenic make-up, probably selected by the antibodies built up against the dominant antigens of previous strains, and that, after a new dominant antigen is acquired, the precursor strain disappears rapidly.

In this respect it is most important to consider the fact that, from the work of Davenport et al. (1953) and from fig. 2, it can be concluded that, after 1918, the human race was in contact with the swine antigen for another 7–13 years. Since, in the cross-H.I. test, antigenic overlapping between the swine strain and the first isolated human influenza strain A/WS (1933 England) is clearly present, it is conceivable that, after 1918, derivatives of the swine strain were circulating, most probably with a different dominant antigen but with an antigenic relationship to swine. Strain analysis after 1933 has further shown that all the main human-strain types which appeared in 1934–56 were probably derived subsequently from a precursor. How far the dominant swine antigen can be "followed" in the strains appearing after 1933 has not yet been investigated carefully enough, and further experiments in this respect should be made in the future. Summarising, we can assume that, so far as the influenza-A group is concerned, the period 1918–56 may be considered as the "swine-influenza" era, even if the dominant swine antigen has vanished for the most part in the isolates found after 1933.

It is not improbable that we may accept the same course of events for the hypothetical influenza-virus of 1889, and that 1889–1918 represents an "Asiatic-influenza" era. Since hypothetical influenza-A strains circulating shortly before 1889 did not represent a "true" pandemic type, it is less probable that the 1957 Asiatic strain should be identical with such a strain, by chance starting a pandemic again in Asia, than to assume that a carriership of a particular A strain in Asia exists, presumably in an animal, causing human pandemics at long intervals of time. In this respect it is worth while to notice also that the "true" pandemics of 1830 and 1782 are considered to have originated in China (Ripperger 1892), and that strains of influenza virus isolated from North American swine in 1930–54 do not show great changes in antigenic composition (Gompels 1953, Jensen and Peterson 1957).

If fig. 1 represents a remnant of the antibody pattern originating in 1889–90, there is no definite evidence of the persistence of the "old" Asiatic antigen for a short period after 1890. It should be emphasised, however, that, if it had been present after 1890, the height of the titres would have been considerably lower than that of those originating in the pandemic itself (compare fig. 2), and that most probably the antibody would have vanished almost completely.

The hypothesis that the Asiatic strain of 1957, or a precursor strain with some antigenic relationship, has been in circulation for a long time, causing only scattered cases of influenza, seems improbable, because it would be very difficult to explain why such a strain should start a true pandemic again in Asia. The same can be argued against the theory that the Asiatic strain has been derived from recent human A strains by mutation.

For all those reasons we believe that the antibody pattern shown in fig. 1 may well have originated in the pandemic of influenza in 1889–90, and that the pandemic of Asiatic influenza in 1957 may have been a repetition of it, emerging from a pre-existing carriership in central Asia.

In the future it may be of importance to test again the present collection of old-age sera against new strains of influenza virus A which may turn up. If by chance the theoretical mutant of the current Asiatic virus which may appear in future should be found to be inhibited by human sera of a younger age-group than 70–100 (in 1957), almost certain proof of the identity of the current strain with that of 1889 could be obtained. At the same time it could be shown that the direction of the possibly developing mutation of the current Asiatic strain was the same as the one manifesting itself after 1890.

Difficult to explain are the facts in table IV. If the post-vaccination increases in H.I. titre against the Asiatic antigen were confined to the age-group 40 or more, they might indicate a stimulation of antibody against a remnant of the Asiatic dominant antigen present in derivative strains of the Asiatic type, which perhaps turned up in 1890–1918, after which the swine strain started to become dominant. This phenomenon is actually seen when people aged less than 20 are vaccinated with the strain A/PR$_8$ (1934 U.S.A.). In some cases post-vaccination titres against the swine strain appear, which can be explained by assuming a small antigenic overlapping of this strain with the PR$_8$ strain (Davenport and Hennessy 1956, Jensen and Peterson 1957, and our own unpublished observations). Since, however, the H.I. antibody against the Asiatic antigen after vaccination with heterologous recent human A strains appears also in persons born long after 1918, this theory cannot completely explain the phenomenon.

A possible explanation could be that there is still a minor overlapping in hæmagglutinating antigen between the Asiatic strain and recent A strains, which cannot be demonstrated with the routine animal antisera and

methods used in the cross-H.I. test but may be shown by a highly sensitive antibody response of some people. The possibility that a minor hæmagglutinating Asiatic antigen may be situated within the virus particle of previous A strains should also be kept in mind. Meyer et al. (1957) came to the same preliminary conclusion when they observed occasional small increases of titre against strains of the Asiatic type in their tests with paired sera from epidemics of previous years in military personnel as well as a few low H.I. titres against the same strains in sera from recruits vaccinated with a mixture of former A strains. The occasional low H.I. titres found by us in persons aged less than 70 may be explained in the same way, although no-one was found associated with a positive C.F. test with soluble antigen or with a previous vaccination. This observation emphasises the need for new experiments in which careful attention should be paid to minor overlapping titres between former A strains (including the swine strain) and the Asiatic type. The use of high-titred animal antisera produced with adjuvant vaccines might perhaps be helpful in these tests.

**Summary**

Pre-epidemic antibody against the 1957 Asiatic influenza virus was found in greatest number and with highest titre in people aged 71 or more living in the Netherlands.

This suggests that the 1957 pandemic of influenza was a repetition of an epidemic which appeared in the last quarter of the 19th century, and that this epidemic might well have been the pandemic of 1889–90, which also originated in Asia.

Similar investigation in the future of a possible mutant of the current Asiatic virus might be of importance to substantiate this theory.

Low increases of antibody titre against the current Asiatic strains were observed in some people in younger and older age-groups after vaccination with monovalent vaccines from former human A strains.

To explain this phenomenon a careful study of eventually existing minor overlapping of hæmagglutinating antigen between the Asiatic strain, former human A strains, and the strain of swine influenza may be helpful.

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# SEROLOGICAL STUDIES WITH ASIAN STRAIN OF INFLUENZA A

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WHEN the virus of Asian influenza was isolated in Singapore in May, 1957, it was found to be an influenza-A strain because it contained the soluble complement-fixing antigen common to all influenza-A strains. It differed from all previous influenza-A strains, however, in that the hæmagglutination-inhibition test, which detects strain-specific antigens, showed no cross-reactions with any previous strain (Jensen 1957, Meyer et al. 1957). This explains the finding that only a very small proportion of people before exposure to the virus had hæmagglutination-inhibiting antibodies against the Asian strain (Meyer et al. 1957, Davoli and Corsi 1957, J. Mulder, personal communication).

This absence of antibodies in the pre-epidemic sera gave a wonderful opportunity for studying the effect of the epidemic of Asian influenza on the serological status of the population. It was first necessary to establish the effect of clinical illness due to the virus on the antibodies demonstrated by the hæmagglutination test. This was done by testing pairs of sera from some patients in various school and other epidemics and from others admitted to hospital with pneumonia and other complications of influenza. A group of university students were also bled five weeks after the epidemic, and the findings were compared with the histories in these persons of illnesses resembling influenza.

Population studies were made by hæmagglutination tests on random sera collected before the outbreak between 1955 and 1957, some of which were pooled by age-group, and on individual and other pooled sera collected in November, 1957, two months after the peak of the epidemic. Sera from patients with influenza in 1949, 1951, and 1956 and from persons inoculated with various influenza-virus vaccines in 1955 and 1956 were also tested by the same methods in the hope of throwing light on the relationship between the Asian-virus antigen and those appropriate to earlier influenza-A viruses.

## Materials and Methods

*Sera* were kept at −26°C for periods of a few weeks to 2 years, except for those collected in 1949 and 1951, which were freeze-dried.

*Viruses.*—The strains of influenza virus used were FM1 1947, A/England/1/51, A/England/211/56 (all representative of past A strains and referred to later as A prime strains), and A/Singapore/1/57. Pools of virus for hæmagglutination-inhibition tests were made by intra-allantoic inoculation of 10-day embryonated eggs with a dilute suspension of virus. After 48 hours' incubation at 35°C the allantoic fluids were harvested, pooled, and stored at −26°C in small bottles.

*Hæmagglutination-inhibition* (H.I.) *tests* were made by a modification of the World Health Organisation's (1953) plastic-plate technique.

*In receipt of a grant from the Medical Research Council.

Phosphate-buffered saline solution (pH 7.2) was used instead of physiological saline solution and all the sera were treated overnight with cholera filtrate. The method of preparing the cholera filtrate and that of treating the sera were as described by Hilleman and Werner (1953). This treatment was necessary because influenza A/Singapore/57 is very susceptible to non-specific inhibitor. In all the experiments, except those on pooled sera and vaccination sera, red cells were obtained from the same fowl. The titre of a serum was expressed as the reciprocal of the initial dilution producing partial inhibition.

*Complement-fixation tests.*—A modification of the method of Fulton and Dumbell (1949) was used, influenza-A soluble antigen being prepared from the chorio-allantoic membrane of eggs infected with the WS strain. The methods used have been described previously (Balducci et al. 1956).

## Results

### *Serological Tests on Pairs of Sera from Patients with Influenza in the 1957 Epidemic*

Both H.I. tests against A/Singapore/57 and complement-fixation tests using an influenza-A soluble antigen were done on 80 pairs of sera from patients with influenza. They included sera from patients in two public schools, an R.A.F. station, the university health service, and employees at a steel works. The remainder (31) were from patients with influenza admitted to hospital mainly with complications—e.g., pneumonia.

Influenza-A virus of Asian type was isolated in eggs from three of these patients and from four of their contacts.

Table I shows the results of the H.I. tests on these sera. It will be seen that most of the acute specimens of serum

TABLE I—HÆMAGGLUTINATION-INHIBITION TITRES OF PAIRS OF SERA FROM CLINICAL CASES OF INFLUENZA

| Category | Phase of illness | No. of sera | Distribution of H.I. titres: | | | | | | | Cases with rises of antibody |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | ≤ 10 | 10–15 | 20–30 | 40–60 | 80–120 | 160–240 | > 240 | |
| Uncomplicated influenza | Acute | 49 | 46 | 3 | .. | .. | .. | .. | .. | 27 (55%) |
| | Convalescent | 49 | 19 | 9 | 6 | 7 | 7 | .. | 1 | |
| Admitted to hospital | Acute | 31 | 10 | 5 | 8 | 4 | 2 | 1 | 1 | 21 (68%) |
| | Convalescent | 31 | 5 | 1 | 5 | 1 | 4 | 5 | 10 | |

from uncomplicated cases of influenza contained no detectable hæmagglutination-inhibiting antibody. The acute specimen of serum was often collected rather late in the illness from the patients admitted to hospital, and antibody was detected in two-thirds of these sera.

The convalescent sera contained antibody in 30 of the uncomplicated cases (61%) and in 26 (84%) of the hospital patients. Fourfold or greater increases of antibody were detected by the H.I. test in 27 (55%) of uncomplicated cases and in 21 (68%) of the hospital patients.

The results of the complement-fixation tests were similar. Most of the acute specimens of serum gave titres of less than 4. Complement-fixing antibody was present in the convalescent serum of 84% of uncomplicated cases and 74% of the hospital patients. Fourfold or greater increases of antibody were detected by the complement-fixation test in 36 (74%) of uncomplicated cases and in 18 (58%) of the hospital patients. Thus in the uncomplicated cases the complement-fixation test was positive more often than the H.I. test.

13% of the patients showed no significant level of antibody in the convalescent serum by either test, a further

TABLE II—HÆMAGGLUTINATION-INHIBITION TESTS ON SERA FROM MEDICAL STUDENTS

| History of clinical influenza | No. positive | No. negative | Total |
|---|---|---|---|
| Yes .. .. .. | 17 | 3 | 20 |
| Doubtful .. .. | 2 | 1 | 3 |
| No .. .. .. | 5 | 19 | 24 |
| Total .. .. | 24 | 23 | 47 |

Sera with titres of 10 or more were considered positive.

7% developed antibody detected only by the H.I. test, and 19% showed complement-fixing antibody only.

From these results it is possible to guess that about 30% of the population of Sheffield who had attacks regarded as clinical influenza had no antibody detected by the H.I. test in their sera during convalescence.

### *Relationship between Positive Hæmagglutination-inhibition Test and History of Clinical Influenza*

In the third week of November, 1957, five weeks after the peak of the outbreak in the university students, single samples of serum were collected from 47 first-year students. At the same time they were asked whether or not they had had illnesses resembling clinical influenza. The results of H.I. tests against A/Singapore/57 on these sera are shown in table II. There was good correlation between a history of influenza and a positive H.I. test.

The results showed that 5 (about 20%) of infections producing hæmagglutination-inhibiting antibody were subclinical. Probably at least the same proportion of all infections, both with and without detectable serological response, were subclinical. The results cited above showed that about 30% of all patients with presumed influenza had no detectable hæmagglutination-inhibiting antibody in their convalescent sera. The figures for the above-mentioned students (4 of 23) are comparable with these. Thus the H.I. test done on a single specimen of serum would detect only 70% of recent cases of clinical influenza but would reveal a further 20% with subclinical infections.

### *Comparison of Antibodies in Population before and after the Asian Influenza Epidemic*

Tests were done to study the effect of the 1957 epidemic on hæmagglutination-inhibiting antibodies to Asian virus in the population of Sheffield and neighbourhood. It was hoped that information would be obtained about the extent of infection in the population during the epidemic.

*Pre-epidemic sera.*—Table III shows the results of the H.I. tests against A/Singapore/57 on 154 sera collected in England before July, 1957. Most of these sera had come from the north of England from suspected cases of toxoplasmosis, 39 were from suspected cases of virus infection from Sheffield, and 19 were from persons aged 80 or more in an old people's home.

TABLE III—RESULTS OF HÆMAGGLUTINATION-INHIBITION TESTS AGAINST A/SINGAPORE/57 ON SERA COLLECTED BEFORE THE EPIDEMIC

| Age (yr.) | No. tested | No. with titres of 10 or more | Titres |
|---|---|---|---|
| 0–9 | 23 | 1 | 80 |
| 10–19 | 21 | 0 | |
| 20–29 | 28 | 1 | 20 |
| 30–39 | 27 | 2 | 10 & 30 |
| 40–49 | 10 | 0 | |
| 50–59 | 13 | 0 | |
| 60–69 | 11 | 1 | 30 |
| 70–79 | 2 | 0 | |
| 80–89 | 18 | 1 | 80 |
| 90–92 | 1 | 0 | |
| Total | 154 | 6 | |

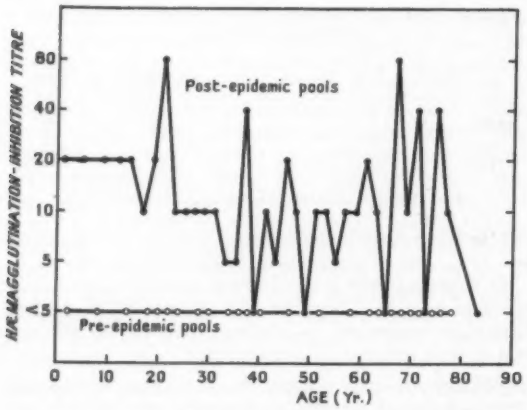


**Fig. 1—Titres of pools of sera tested against A/Singapore/57.**

6 of the sera gave titres of 10 or more. They were from persons of various ages, and only one of these belonged to the old-age group. In repeat experiments the numbers of such sera varied with the batch of cholera filtrate used, and in one experiment, in which a particularly weak batch was used, 25 sera gave positive results. Neutralisation tests were not done; so it was impossible to decide whether the six sera actually contained antibody against the Asian strain or whether the result was due to non-specific inhibitor. In addition to these, none of the sera taken from the 168 persons before vaccination in 1955 and 1956 (see below) contained inhibitor against the Asian strain. These people were mostly young adults.

Besides these individual sera, pools of sera collected in 1955 were tested by hæmagglutination-inhibition against A/Singapore/57. The sera had been pooled according to age in two-year age-groups, up to 50 sera being put into each pool. 25 of the pools between the age of 2 and 78 were tested (fig. 1), and all had titres of less than 5. This was very different from the results obtained with similar serum pools collected in 1954 in Sheffield and tested against other viruses (Davenport et al. 1955). It thus appears that most of the sera from the population of Sheffield were devoid of detectable antibody against the Asian strain before the outbreak.

*Post-epidemic sera.*—The peak of the epidemic in Sheffield was during the week ending Sept. 21, 1957. Between Nov. 1 and Nov. 30, 1957, 1660 sera were collected by the Sheffield Blood Transfusion Service, the Sheffield Public Health Laboratory, and the pathological laboratories of many of the Sheffield hospitals. Most of them came from blood-donors or were sent for Wassermann tests, the rest being sent to the laboratories for various routine tests. All these sera were tested after pooling according to age, and many were also tested individually.

637 sera were tested individually against the A/Singapore/57 virus (fig. 2). 283 (44%) had titres of 10 or more. The percentage of sera positive in each 10-year age-group was 16–71%, being highest under the age of 20 and lowest between the ages of 60 and 69. This variation may reflect the attack-rate in the different age-groups but may also have been partly due to the fact that different pools of antigen were used in the various tests.

All the 1660 sera (including those tested individually) were pooled according to age as follows: (1) between the ages of 17 and 76 they were pooled in 2-year age-groups; (2) the age ranges of the remaining pools were 0–3, 4–7, 8–11, 12–13, 14–16, 77–79, and 80–88; and (3) each pool consisted of 50 sera, except those from persons aged less than 16 and persons aged more than 66, which contained 21–47 sera.

All the pools were tested by hæmagglutination-inhibition against A/Singapore/57 at the same time that the 1955 pools were tested. Thus in one experiment, using the same antigen, red cells, and cholera filtrate, the age-distribution of antibody against the Asian virus was determined in 1660 post-epidemic sera. The results are shown in fig. 1. There was considerable variation from pool to pool, and there was no obvious trend with age. But there was a remarkable difference in the results of the tests against A/Singapore/57 virus with the sera collected before and after the epidemic.

*Cross-hæmagglutination-inhibition Tests*

*With sera from cases of influenza.*—Table IV shows the results of tests on acute and convalescent specimens of serum from patients with influenza in 1949, 1951, 1956, and 1957. None of the sera collected before 1957 showed rises in inhibition titre against A/Singapore/57, although

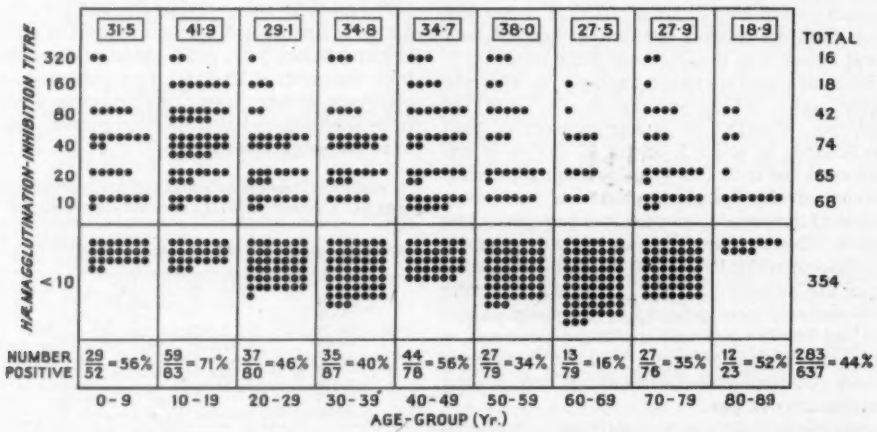


**Fig. 2—Post-epidemic sera tested against A/Singapore/57. Numerals in rectangles denote geometric means of sera with titres of 10 or more.**

TABLE IV—TESTS ON PAIRED SERA FROM PATIENTS WITH INFLUENZA IN 1949, 1951, 1956, AND 1957

| Case no. | Titres in complement-fixation test v. soluble antigen | Hæmagglutination-inhibition titres against: | | | |
|---|---|---|---|---|---|
| | | FM1 | A/Eng./51 | A/Eng./56 | A/Sing./57 |
| *1949:* | | | | | |
| 1 | 0/48 | 0/30 | | | 0/0 |
| 2 | 0/>64 | 0/120 | | | 0/0 |
| 3 | 16/>64 | 0/240 | | | 0/0 |
| *1951:* | | | | | |
| 1 | 0/48 | | 0/30 | | 0/0 |
| 2 | 0/32 | | 0/7·5 | | 0/0 |
| *1956:* | | | | | |
| 1 | 0/16 | | | 0/15 | 0/0 |
| 2 | 0/24 | | | 0/30 | 0/0 |
| 3 | 0/48 | | | 0/7·5 | 0/0 |
| 4 | 0/>64 | | | 0/160 | 0/0 |
| 5 | 0/16 | | | 0/7·5 | 0/0 |
| 6 | 8/32 | | | 0/15 | 0/0 |
| *1957:* | | | | | |
| 1 | 0/48 | | | 0/0 | 0/30 |
| 2 | 0/>64 | | | 0/0 | 10/>320 |
| 3 | 0/6 | | | 0/0 | 0/30 |
| 4 | 0/64 | | | 30/20 | 0/15 |
| 5 | 6/48 | | 60/20 | 15/<10 | 0/30 |
| 6 | 0/24 | | 15/30 | 0/15 | 0/80 |
| 7 | 0/48 | | 10/10 | 7·5/7·5 | 0/15 |
| 8 | 0/48 | | 10/10 | <10/0 | 0/30 |
| 9 | 0/24 | | 80/60 | 7·5/7·5 | 0/15 |
| 10 | 6/>64 | | 0/60 | 7·5/60 | 0/120 |
| 11 | 0/48 | | 60/60 | 120/120 | 0/120 |

0: less than 4 in the complement-fixation tests and less than 5 in the hæmagglutination-inhibition tests.

all showed rises in titre against the strains prevalent at the time of collection. Most of them were from young adults. 11 pairs of sera from patients with influenza in the 1957 epidemic which showed rises in titre against A/Singapore/57 were tested against A/England/51 and A/England/56. Whereas some of these sera contained antibody against these " A prime " strains, in only 2 cases was there a rise in titre. This shows that anamnestic reactions, such as occur between influenza-" A prime " and influenza-A strains (Stuart-Harris and Miller 1947), can also occur between the Asian virus and " A prime " strains.

*With sera from vaccinated persons.*—H.I. tests against A/Singapore/57 were done on 168 pairs of sera from people vaccinated with one dose of influenza vaccine in 1955 and 1956. The first specimen was taken before vaccination and the second about four weeks after. For those given oil adjuvant vaccines a third specimen was taken three months after vaccination. 32 persons were given a monovalent vaccine containing A/England/54, 15 a monovalent vaccine containing A/Malaya/54, 14 a monovalent vaccine containing A/England/55, 42 a monovalent oil adjuvant vaccine containing A/England/56, and 65 a polyvalent vaccine containing swine, PR8, and FM1 influenza-A viruses. Most of the subjects were aged 18–25, but 7 given the polyvalent vaccine, 7 given the A/England/54 vaccine, and an unknown number given the A/England/56 vaccine were aged more than 25. Most of the 168 sets of sera had shown rises in titre by the H.I. test against the homologous antigen.

The H.I. titres of pre- and post-vaccination specimens from 160 of the vaccinated persons were less than 10. In the remaining 8 sets of sera (5%) the titres of the first specimen were less than 10 and those of the second or third were 15 (4 instances), 20, 30, and 40 (2 instances). 4 of these titres were confirmed on repetition. 2 of the sera were from persons given the polyvalent vaccine and 6 the A/England/56 monovalent vaccine.

It thus appears that inhibitor against the Asian-virus antigen was occasionally stimulated to appear in the serum after immunisation with a single injection of vaccine made from an influenza virus recovered before 1957. Our inability to detect similar appearances of inhibitor after infection with the latter viruses may have been due to the small number of available sera tested. Meyer et al. (1957) detected inhibitor to the Asian virus in sera from some patients with clinical influenza before the Asian epidemic. Such naturally developing antibody would explain our own finding of occasional inhibitor to the Asian virus antigen in the pre-epidemic sera.

## Discussion

The serological results obtained in Sheffield in cases of Asian influenza are similar to those found during previous epidemics of influenza A and are in conformity with the results of other workers. The H.I. test using the Singapore virus showed a rise of antibody in 60% and the complement-fixation test in 68% of cases. The corresponding results obtained during the 1951 epidemic were that H.I. tests with the appropriate virus antigen were positive in 59% and complement-fixation tests using soluble antigen were positive in 75% of cases (Stuart-Harris 1953). During the Asian epidemic the H.I. test detected antibody in convalescence in 70% of clinical illnesses but also indicated subclinical infection in 20% of the population. Lim et al. (1957) found in Singapore that the H.I. test detected antibody in 67% of patients with Asian influenza admitted to hospital and revealed subclinical infection in 13% of persons who remained symptom-free.

The study of the distribution in the population of Sheffield of antibody detected by the H.I. test after the epidemic showed that at least 16–71% of persons of various ages had become infected. Even 30–50% of those aged 70 or more showed evidence of infection. The appearance of antibody in a high proportion of young adults and children agreed well with the numbers of illnesses observed by practitioners. However, many doctors in Sheffield commented that there were relatively fewer illnesses in those aged more than 40, and the attack-rate in Beckenham measured by Fry (1958) fell progressively after the age of 20. It seems likely that many infections in the older persons in Sheffield were either very mild or asymptomatic. The average attack-rate in the population which could be surmised from these serological results was at least 50%.

The geometric mean titres of antibodies found at various ages in the post-epidemic period, if we ignore the sera which did not inhibit agglutination at 1 in 10 dilution, showed relatively little variation with age (fig. 1). The highest mean titre was in the second decade, and that in persons aged more than 60 was not so high. This appeared to indicate a relatively uniform serological response to infection such as would be expected if the Asian-virus antigen had not been experienced previously by those who became ill.

The finding of inhibitor to the Asian virus in 6 of 322 sera collected before the epidemic has to be considered in association with the observed appearance of inhibitor in 8 of 168 persons immunised with various influenza-virus vaccines which did not contain Asian virus. We have no proof that the inhibitor was neutralising antibody, but the assumption that this was so is reasonable. These instances of serum inhibition were infrequent and bore no apparent relation to age. Mulder (1957) has brought forward evidence that antibody to the Asian virus was

present in Holland in some aged persons before the epidemic and was rare in persons aged less than 80. He also observed (personal communication) the development of antibody after immunisation with an influenza vaccine which did not contain the Asian strain. Our own results do not entirely conform with Mulder's view that the Asian virus is essentially the virus responsible for the 1890 pandemic. An alternative explanation is that the Asian virus shares a minor antigenic component with some of the influenza viruses experienced before 1957. This minor component might represent the survival of a major antigen from some virus causing a human pandemic in the past. It could form the basis for a genetic variation in which the minor component had become the major antigen recognised in 1957 as that of the Asian virus.

**Summary**

H.I. antibody to the Asian influenza-virus antigen was detected in 70% and complement-fixing antibody to the soluble A antigen in 80% of convalescent sera from 80 cases of influenza with or without complications in Sheffield during the 1957 epidemic of Asian influenza.

In 47 students H.I. tests on sera taken after the epidemic showed that 20% of infections were asymptomatic.

6 of 322 sera collected before the epidemic contained inhibitor to the Asian virus. 283 (44%) of 637 sera collected after the epidemic in Sheffield contained inhibitor, the number varying between 16% and 71% in persons of different ages.

Pools of sera collected before 1957 and assembled by age showed no H.I. antibody to the Asian virus. Similar pools of sera collected after the epidemic showed antibody in amounts varying within wide limits. Probably at least half the population had been infected during the epidemic.

H.I. antibody against the Asian virus appeared in the serum of 8 of 168 persons vaccinated with "A prime" and polyvalent vaccines but was not detected in the convalescent sera from 11 patients with influenza before 1957.

The significance of the results is discussed in regard to the relationship between the Asian and other influenza-A viruses.

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# STRAIN-SPECIFIC COMPLEMENT-FIXATION TEST IN ANTIGENIC ANALYSIS AND SERODIAGNOSIS OF INFLUENZA *

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DIFFICULTIES have arisen in the use of the hæmagglutination-inhibition test for antigenic analyses of strains of influenza virus by specific immune sera and for strain-specific serodiagnosis.

Uncertainty in the interpretation of the results has been introduced by: (1) phase variations in the viruses, on adaptation to laboratory hosts, as regards the degree of agglutination or the species of red cells agglutinated; and (2) differential susceptibilities of strains to one or more of the non-specific inhibitors present in immune sera derived from different animals. Though several techniques are used for removing inhibitors from sera, none is universally successful, and there is no assurance that specific antibody levels remain unaffected. For these reasons other methods of determining antigenic patterns and strain-specific antibody responses were sought.

The complement-fixation test (C.F.T.) is highly satisfactory for these purposes so long as the type-specific soluble antigen (S) common to all strains of one type and the strain-specific virus antigen (V) are clearly separated. Equally essential is the use of anti-S sera free from anti-V (for proving absence of S in V) and, conversely, of anti-V sera devoid of antibodies to S. These requirements have not generally been met in the past, but these reagents can now be produced regularly. The non-specific inhibitors of hæmagglutination do not interfere with the C.F.T.

## Methods

The *S-antigen* is obtained by exposing virus particles to ether (Hoyle 1952, Lief and Henle 1956a). The internal S thus released is freed from all V by exhaustive adsorption on to chicken and guineapig red cells.

*Anti-S sera* are produced by intranasal inoculation of guineapigs with small doses of active virus, followed after five or more weeks (when initially formed anti-V has disappeared) by an intraperitoneal injection of S prepared from a distantly related homotypic strain. Thus only anti-S is boostered (Lief et al. 1958).

Virus particles separated from infected allantoic fluids by two cycles of adsorption on to and elution from red cells are suitable as *V antigens* for C.F.T., since such suspensions are usually free from external S (Lief and Henle 1956b).

Guineapig *anti-V sera* are produced by three or more intraperitoneal injections of the hæmagglutinin fraction (devoid of external and internal S) obtained from ether-treated elementary bodies by the red-cell adsorption-elution procedure (A. Fabiyi, F. S. Lief, and W. Henle, unpublished).

## Results

Cross-matching of V antigens of 36 type-A strains, isolated between 1931 (swine influenza S-15 strain) and 1957 (A-Japan-305), with the corresponding anti-V sera in block titrations revealed antigenic patterns in general

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TABLE I—ANTI-V RESPONSES IN SELECTED PATIENTS OF $A_1$ AND ASIAN INFLUENZA

| Case no. | Age (yr.) | Virus | Days after onset | Serum titres v. antigens | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | S-15–V 1931 | PR8–V 1934 | $F_{11}$–V 1940 | $L_2$–V 1947 | Phila.–V 1953 | $NL_1$–V 1957 | Asian–V 1957 | S type A | Lee–V type B |
| 1 | 10 | $NL_2$ | 8/22 | 8/16 | 8/32 | 0/4 | 32/64 | 32/128 | 32/256 | 0/4 | 0/32 | 0/0 |
| 2 | 13 | ,, | 3/17 | 0/16 | 0/32 | 0/8 | 0/128 | 8/128 | 0/128 | 0/4 | 8/96 | 0/0 |
| 3 | 13 | ,, | –/15 | –/32 | –/32 | –/16 | –/128 | –/128 | –/128 | –/16 | –/128 | –/8 |
| 4 | 16 | ,, | 4/18 | 0/32 | 8/64 | 0/24 | 8/128 | 8/128 | 0/128 | 0/8 | 32/256 | 0/0 |
| 5 | 39 | ,, | 2/16 | 8/64 | 0/32 | 8/24 | 0/32 | 0/64 | 0/64 | 0/128 | 8/64 | 0/0 |
| 6 | 47 | ,, | 2/16 | 32/64 | 16/64 | 8/32 | 8/48 | 8/48 | 0/32 | 0/64 | 12/64 | 16/16 |
| 7 | 52 | ,, | 1/15 | 12/64 | 8/128 | 0/64 | 8/128 | 0/256 | 0/256 | 4/12 | 8/256 | 0/0 |
| 8 | 1 | Asian | 1/8 | 0/4 | 0/0 | 0/4 | 0/0 | 0/0 | 0/0 | 4/96 | 0/48 | 0/0 |
| 9 | $1^1/_2$ | ,, | 3/24 | 0/192 | 0/24 | 0/24 | 4/192 | 8/128 | 16/256 | 8/256 | 4/128 | 0/0 |
| 10 | 4 | ,, | 3/17 | 0/24 | 0/12 | 0/24 | 0/48 | 8/48 | 8/128 | 0/128 | 0/64 | 0/0 |
| 11 | 63 | ,, | 9/19 | 16/32 | 0/0 | 0/0 | 16/4 | 0/0 | 0/0 | 6/256 | 6/256 | 0/0 |
| 12 | 77 | ,, | 4/39 | 0/96 | 0/0 | 0/48 | 0/64 | 0/48 | 0/96 | 0/128 | 0/96 | 0/0 |
| 13 | 84 | ,, | 1/15 | 0/32 | 0/0 | 0/24 | 4/32 | 4/48 | 4/96 | 0/96 | 0/32 | 0/0 |
| Anti-S (type A) | | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 256 | 0 |

• 0 = < 1 : 4

agreement with those obtained in other laboratories by hæmagglutination-inhibition methods (Hirst 1952, Hilleman 1951, Jensen and Francis 1953). The anti-Asian V serum (A-Japan-305) reacted to some extent with WS (1933) V; and anti-V sera to a 1951 and 1953 strain fixed complement to low titres in the presence of Asian V. Such " one-way cross-reactions ", seen also in other combinations and often extending over several type-A families of strains, may reflect differences in the in-vitro and in-vivo antigenicity of some components.

The strain-specific anti-V sera were effective in the rapid identification of new isolates of virus during outbreaks of $A^1$ and Asian influenza in 1957. In most cases the identity and antigenic relationships were established with first chick embryo-passage materials, so long as the amniotic or the allantoic fluids contained more than 20 hæmagglutination units per ml. (F. S. Lief, M. Ostapiak, A. Fabiyi, and W. Henle unpublished). Rarely three chick embryo passages were required before these determinations were feasible.

The V antigens were found suitable for strain-specific serodiagnosis of influenza (F. S. Lief and W. Henle, unpublished). More than 90% of more than 800 cases of Asian influenza revealed significant increases in antibodies to the specific V antigen. An increase in type-specific anti-S was noted in all cases except those in very young children. In most instances it preceded development of anti-Asian V because, most likely, it represented usually a recall. Absence of anti-V responses was referable to premature collection of convalescent blood.

The anti-V responses during the Asian influenza epidemic and the preceding $A^1$ outbreak were rarely restricted to the infecting viruses; if they were, it was mainly in very young patients. The spectrum of these responses was by no means limited to strains circulating during the life-span of the individual. Table I presents the serological data in a few selected cases. None of the patients had anti-V to the infecting strains in the acute-phase sera, so long as the samples of sera were taken in the first few days of illness, but all the convalescent sera were positive. Reactions with other V antigens in the acute-phase sera reflected to some extent the patient's age, in that positive results with early strains, such as S-15 and PR8, were noted mainly in older age-groups; but there were exceptions—e.g., cases 1 and 4. Yet in the convalescent sera responses were observed in many cases to V-antigens prevalent before the patient's birth. In a considerable number of the $A^1$ infections (about 35%) in addition antibodies developed to Asian V before this agent appeared. These reactions showed no apparent relation to the patient's age. Such responses were recorded previously in $A^1$ patients (Meyer et al. 1957) and persons immunised with pre-Asian influenza vaccines (Mulder and Masurel 1958).

The results obtained with the acute-phase sera appear to be in agreement with those of previous antibody surveys using hæmagglutination-inhibition tests (Mulder and Masurel 1958, Davenport et al. 1953, Hennessy et al. 1955) in that, with increasing age, antibodies to progressively earlier strains were found. This has been interpreted to mean that the virus responsible for the initial influenza in childhood determines the antibody responses to subsequent exposures to antigenically different strains and, with it, the antibody patterns found throughout life. If this interpretation is correct, the results suggest that the pandemic of 1918–19 was caused by a strain of what is now known as swine influenza virus (Shope 1936), and that of 1888–89 by an agent closely related to Asian influenza virus (Mulder and Masurel 1958); but the fact that some relatively young patients responded with antibodies to the S-15, PR8, and Japan-305 strains cannot be overlooked. The development of anti-V in a patient to strains to which he could not possibly have been previously exposed suggests other interpretations.

A broadening of antibody responses in animals after

TABLE II—ANTI-V RESPONSES IN GUINEAPIGS AFTER SUCCESSIVE INFECTIONS WITH DIFFERENT STRAINS OF INFLUENZA-A VIRUS

| Exposure | | Weeks after start | Serum titres v. antigens | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Case no. | Strain | | S-15-V 1931 | PR8-V 1934 | $F_{11}$-V 1940 | $L_2$-V 1947 | Phila.-V 1953 | $NL_1$-V 1957 | Asian-V 1957 | S type A | Lee-V type B |
| 1 | S-15 | 0/3 | 0/128• | 0/0 | 0/16 | 0/0 | 0/0 | .. | .. | 0/128 | 0/0 |
| 2 | PR8 | 21/24 | 0/256 | 0/256 | 0/256 | 0/128 | 0/64 | .. | .. | 0/512 | 0/0 |
| 3 | $F_{11}$ | 36/39 | 128/256 | 64/64 | 64/192 | 24/48 | 0/12 | .. | .. | 128/192 | 0/0 |
| 4 | $L_2$ | 49/53 | 128/128 | 64/128 | 64/128 | 24/128 | 12/16 | 0/32 | 0/48 | 128/128 | 0/0 |
| 1 | PR8 | 0/3 | 0/0 | 0/64 | 0/0 | 0/0 | 0/0 | .. | .. | 0/64 | 0/0 |
| 2 | $F_{11}$ | 10/13 | 0/0 | 32/64 | 8/64 | 0/32 | 0/0 | .. | .. | 0/128 | 0/0 |
| 3 | $L_2$ | 26/30 | 0/8 | 32/256 | 32/128 | 12/256 | 0/32 | 0/16 | 0/12 | 64/128 | 0/0 |
| Anti-S (type A) | | — | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 256 | 0 |

Serum titre at time of exposure/titre 3–4 weeks later.

repeated infections or intraperitoneal injections of active virus has been observed in early studies (see Van Rooyen and Rhodes 1948). This problem was reinvestigated by repeated intranasal inoculations of guineapigs at intervals of ten to twenty-one weeks with active influenza viruses of progressively later vintage or even with the same strain:

The first exposure usually induced strain-specific anti-V responses—i.e., to the homologous and closely related strains.

On second and subsequent exposures these antibodies were recalled and, in addition, whether the same or different viruses were used for reinoculations, the antibody spectra rapidly broadened. The examples offered in table II revealed that ultimately antibodies were formed to V antigens which were not detectably represented in the infecting strains, including Asian V.

It was noted also that, after second or third exposures, the ensuing antibody levels declined at slower rates than after the first infection.

The anti-V reactions observed at the time of the third or fourth exposures were not restricted to the viruses used for previous inoculations.

### Discussion

These results indicate that influenza strains contain a multiplicity of antigens. The dominant, and possibly also the minor, directly detectable components determine the antibody responses on primary infection (Jensen and Francis 1953). Recall of these antibodies on subsequent exposures to different type-A viruses, as well as the anti-V responses to antigens not measurable in the infecting agents, suggests that most, if not all, of the various antigenic components are present mainly at submeasurable levels in any of the strains. Because of the low concentration of most of the antigens several exposures are required before many of the antibodies appear in the serum.

If these observations apply to man, the presence of antibodies to a wide spectrum of V antigens may reflect in part the multiplicity, and possibly spacing and severity, of previous exposures, and not only the antigenic structure of the virus responsible for the primary infection. The older the person, the more influenza infections he is likely to have experienced in the past. The presence of antibodies to swine or Asian influenza viruses in the older age-groups does not necessarily denote, therefore, that they had been infected with these specific agents at the time of the agents' prevalence. Multiple infections with other strains at later dates also could have ultimately produced these antibodies. This problem may be resolved in the future, depending on whether the age-distribution of antibodies to early strains will remain unchanged in ten or more years, or whether anti-S-15 or anti-PR8 reactions will be found gradually in higher age-groups.

It remains to be shown that the various anti-V reactions recorded reflect immunity. If so, present immunisation procedures for man deserve reconsideration. It has been observed that guineapigs, after as many as six intraperitoneal injections of non-infectious hæmagglutinin fractions, still yield strain-specific sera, whereas, as shown above, a few intranasal instillations of active virus induce broad responses, covering antigens not only of past but also subsequent prevalence.

### Summary

A new technique is described for the antigenic analysis of influenza viruses and serological diagnosis of influenza. The method, a strain-specific complement-fixation test with the V (or viral) antigen, avoids the problems of non-specific inhibitors and antibody-virus avidity which make the interpretation of the hæmagglutination-inhibition test so difficult.

By means of this technique it was possible to type Asian viruses rapidly and to achieve a positive serological diagnosis in more than 90% of 800 paired sera. The antibody responses, however, were rarely restricted to the infecting strain, and were in many cases broad enough to cover strains prevalent before the birth of the patients.

Experimentally, it was found that guineapigs infected repeatedly with the same strain or with strains of progressively later vintage gradually developed a broadening antibody response which embraced strains not included in the infecting strains—e.g., the Asian strain.

It is concluded that antibody to Asian virus does not necessarily denote infection with that particular strain at the time when this virus was prevalent but could be produced by multiple infection with other strains at later dates.

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## A SEROLOGICAL TRIAL OF ASIAN-INFLUENZA VACCINE AFTER THE AUTUMN EPIDEMIC *

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SEROLOGICAL trials of an influenza vaccine prepared from the Asian strain before the epidemic, showed, in contrast to previous experience (Beveridge 1944), that two doses were needed for a good serological response (Medical Research Council 1958, Commission on Influenza 1957). A further trial was therefore arranged in November, after the epidemic, by the Directorate of Hygiene and Research of the Royal Air Force at the request of the Medical Research Council's Committee on Influenza and other Respiratory Virus Vaccines.

The object of this trial was to determine the serological response to one and two inoculations of the above vaccine in volunteers who had been exposed, but not ill, and in those who had had influenza in the autumn epidemic.

* A report to the Medical Research Council Committee on Influenza and other Respiratory Virus Vaccines.

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GEOMETRIC MEAN TITRES AND RISES OF HÆMAGGLUTINATING ANTIBODY

| — | No. of doses of vaccine | Geometric means (reciprocal of titre) | | | | | | | | Rises | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Initial titre ⩽ 1/5 • | | | | Initial titre > 1/5 | | | | Initial titre ⩽ 1/5• | | Initial titre > 1/5 | |
| | | No. of volunteers | 1st sample | 2nd sample | 3rd sample | No. of volunteers | 1st sample | 2nd sample | 3rd sample | 1st to 2nd | 1st to 3rd | 1st to 2nd | 1st to 3rd |
| History of influenza-like illness | 1 | 7 | ⩽ 5 | 38 | 37 | 9 | 39 | 216 | 127 | ⩾ 7·6 | 7·4 | 5·5 | 3·3 |
| | 2 | 5 | ⩽ 5 | 38 | 89 | 12 | 35 | 191 | 232 | ⩾ 7·6 | 18·0 | 5·5 | 6·6 |
| No history of influenza-like illness | 1 | 20 | ⩽ 5 | 16 | 21 | 5 | 18 | 111 | 86 | ⩾ 3·2 | 4·2 | 6·2 | 4·8 |
| | 2 | 18 | ⩽ 5 | 28 | 122 | 7 | 35 | 202 | 214 | ⩾ 5·6 | 24·4 | 5·8 | 6·1 |
| All volunteers | 1 | 27 | ⩽ 5 | 20 | 21 | 14 | 29 | 170 | 110 | ⩾ 4·0 | 4·2 | 5·9 | 3·8 |
| | 2 | 23 | ⩽ 5 | 30 | 113 | 19 | 35 | 196 | 225 | ⩾ 6·0 | 22·6 | 5·6 | 6·4 |

• Where result was quoted as being < 1/10, it was assumed to be ⩽ 1/5.

The vaccine was prepared from A/Singapore/1/57, containing about 7000 hæmagglutinating units per dose of 1 ml., by Dr. F. Himmelweit of the Wright-Fleming Institute.

## Material and Methods

Two Royal Air Force stations with different attack-rates during the epidemic were chosen for the trial. Station A, which had a mild outbreak causing an admission-rate to sick quarters of 12%, provided 26 volunteers who had had no clinical respiratory illness during the epidemic. Station B had a severe outbreak of influenza A (Asian) with an admission-rate to sick quarters of 40%. 57 airmen from this station volunteered: 33 of these had had a clinical illness resembling influenza during the epidemic; the rest had not been ill.

All these volunteers received one dose of vaccine. Half of each group, picked by use of a table of random numbers, received a second similar dose three weeks later. Members of each group were bled (into evacuated 'Venules') before the first inoculation, and again at intervals of three and six weeks. The serum was separated and stored at –20°C. When all samples had been collected they were divided at random between the laboratories of Mill Hill and Sheffield, where the serological tests were made. Those testing the sera did not know from which group the samples had been obtained. Anti-hæmagglutination tests were performed with the A/Singapore/1/57 virus and the sera treated with *Vibrio choleræ* extract, according to the recommendations of the W.H.O. expert committee (World Health Organisation 1953).

There was no respiratory illness among the volunteers during the period of the trial. It was found that of those with no clinical history of influenza during this epidemic only 24% had antibodies before inoculation, whereas 64% of those with a clinical history of influenza had antibodies before inoculation.

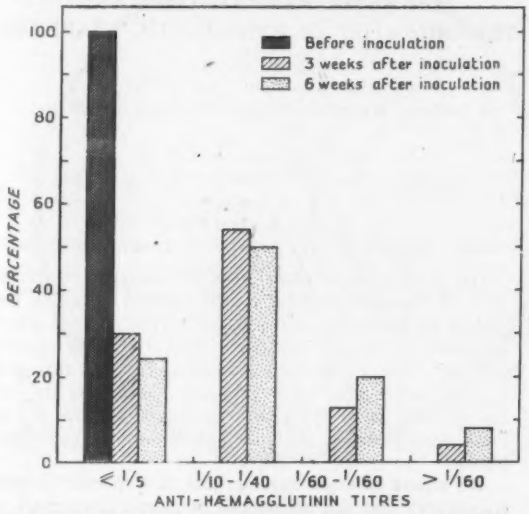


**Fig. 1—Distribution of titres 3 and 6 weeks after a single inoculation of vaccine in 27 individuals with initial antibody titres of ⩽ 1/5.**

## Results

The antihæmagglutination titres in the vaccinated individuals are summarised in the table and figs. 1–4. The titres are shown in the figure as the percentages of individuals with titres within a given range; and figs. 1–4 show antibody distributions in individuals with initial antibody titres of 1 in 5 or lower and in those with initial titres higher than 1 in 5, inoculated with one or with two doses of vaccine.

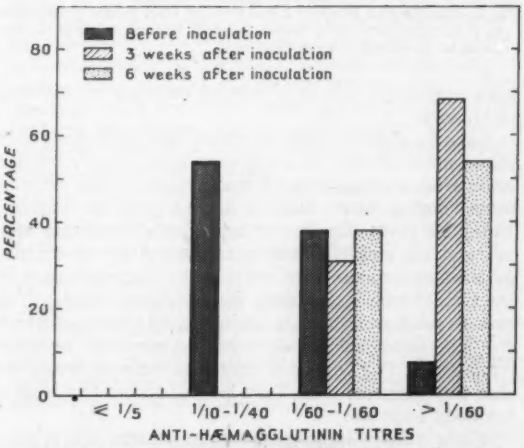


**Fig. 2—Distribution of titres 3 and 6 weeks after a single inoculation of vaccine in 14 individuals with an initial antibody titre of > 1/5.**

The table and fig. 1 show that people with no initial anti-hæmagglutinin reacted poorly to a single dose of Asian vaccine. This finding agrees with the results of many other workers—e.g., Commission on Influenza (1957), Medical Research Council Committee on Influenza and other Respiratory Virus Vaccines (1958).

On the other hand, a single inoculation of the same vaccine gave a much better response in individuals with initial titres of 1 in 5 or more (fig. 2) due to virus-A infection—in most cases associated with a clinical attack of influenza in the epidemic. This is also illustrated in the table, showing a higher geometric mean titre after inoculation. This suggests that previous experience with this antigen had sensitised the antibody-producing mechanism, and in support of this the results in fig. 3 and the table indicate that two inoculations of vaccine, given at an interval of three weeks to individuals without initial antibody, led to a good *secondary* response. Comparison of figs. 1 and 3 shows that the high titres after two inocula-

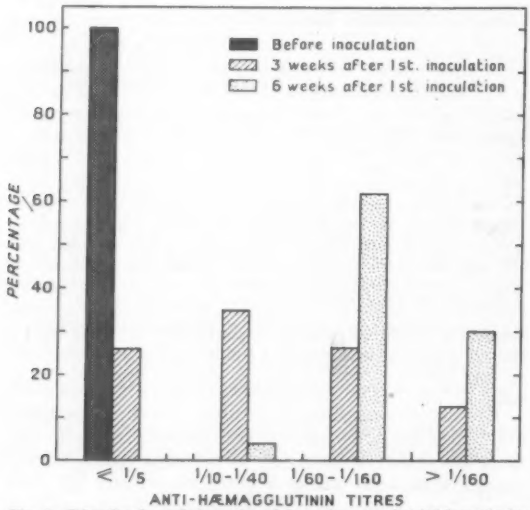


**Fig. 3—Distribution of titres 3 and 6 weeks after initial inoculation in 23 individuals with an initial antibody titre of ⩽ 1/5, given two doses of vaccine at 3-week intervals.**

tions cannot be due to a delayed response to the first inoculation.

From fig. 4 and the table it is clear that individuals with initial antibody titres of 1 in 5 or more received a booster effect from a single dose of vaccine but did not develop much higher titres from a second dose of vaccine. Beveridge (1944) found that individuals vaccinated with BEL and LEE strains of influenza virus A and B did not get a better response from two doses of vaccine given at an interval of two weeks than from a single dose. The present results confirm his conclusion for viruses of which the inoculated individuals have had previous antigenic experience. But with new influenzal antigens it appears that two antigenic stimuli are needed to produce a good antibody response.

These results indicate the requirements for a good serological response, but they tell us nothing of the requirements for protection. Unfortunately the clinical trials designed to compare one dose with two doses of

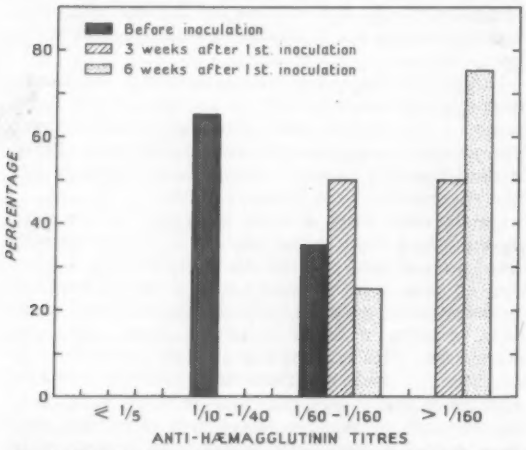


**Fig. 4—Distribution of titres 3 and 6 weeks after initial inoculation in 19 individuals with initial antibody titres of > 1/5, given two doses of vaccine at 3-week intervals.**

Asian vaccine could not be carried out because the epidemic came too early.

This, and most other serological trials, measured only hæmagglutination-inhibition antibody, and it is not known what relation this may have to protective antibody; nor indeed whether protection is due to circulating antibody or to the sensitisation of the protective mechanism—of which the antibody response may only be an indication. Evidence that one injection of Asian-influenza vaccine may provide sufficient protection is given by the result of the M.R.C. trial, which gave a protection-rate of 52–67% immediately after vaccination; this compares well with previous trials in individuals who had previously experienced related influenza-A antigens (Commission on Influenza 1944).

**Summary**

A serological trial of an Asian-influenza vaccine was carried out in 83 volunteers, all of whom had been exposed to the autumn influenza epidemic. 33 had had a clinical illness resembling influenza. Volunteers with no initial antihæmagglutinin reacted poorly to a single dose of vaccine. A much better serological response was obtained with a single dose in individuals with initial titres of 1 in 5 or more. Two inoculations given to individuals without initial antibody led to a good secondary response. This is contrary to previous experience, and it is suggested that two antigenic stimuli are needed to produce a good antibody response in people who have not previously experienced this antigen, whereas one is probably sufficient for those that have.

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# DIABETIC RETINOPATHY AND NEPHROPATHY IN PANCREATIC DIABETES

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THE ætiological relationship of the vascular complications of diabetes mellitus to the disorder itself is the subject of much interest and controversy. In a panel discussion on this problem, LeCompte (1957) has recently said that there is little evidence against the view that they may be determined by the same gene, since there are very few reported cases of capillary lesions in diabetes due to some known cause, such as pancreatitis or pancreatic fibrosis.

We report here the development of a specific diabetic retinopathy and the occurrence of glomerulosclerosis of the type specific to diabetes mellitus, in a patient whose

diabetes is believed to have been due to chronic pancreatitis, and we discuss the implications of these findings.

## Case-report

A man, aged 48, an architect, was said to have had "nephritis" following mumps in 1920, at the age of 11, and for a few years after this had experienced episodes of vague abdominal discomfort. In 1928, when he was 19, he developed the classical symptoms of diabetes mellitus, was found to have considerable glycosuria, and was treated by dietary restriction and the administration of insulin. Except when he had a severe infection, the daily dose of insulin varied from 28 to 40 units.

In 1936 he noticed that his stools were pale and floated in water, and that he had lost weight. In 1947 he complained of episodes of nocturnal diarrhœa, with the incontinent passage of pale fluid fæces. In 1952 he had developed neuropathy in his legs, with absence of ankle reflexes, diminution of knee reflexes, some wasting of the calf and adductor muscles, loss of appreciation of vibration and pain, and absence of sweating in the lower limbs. At this time diabetic retinopathy was first detected; a few microaneurysms and one or two round specks of hyalinisation were visible in both retinæ. In the next two years two classically painless indolent ulcers developed on his feet; he became impotent and was found to have a large distended bladder, unassociated with discomfort, which could not be voluntarily evacuated. The dynamics and chemistry of the cerebrospinal fluid (C.S.F.) were normal and the Wassermann and Kahn reactions of serum and C.S.F. negative. Many courses of various antibiotics were given for urinary tract infections. A little protein was discovered in the urine for the first time in association with the infection. In 1957, incontinence and recurrent infection became so severe that both ureters were transplanted to an isolated loop of ileum which acted as a reservoir, but in spite of this the patient died within a few months of urinary tract infection, toxæmia, and uræmia. At the time of death he had moderately severe diabetic retinopathy (fig. 1). During the last two years of his life his blood-pressure was about 150/105 mm. Hg; there was never any evidence of congestive heart-failure.

During the thirty years of his diabetic life, hypoglycæmic episodes were exceptionally frequent, occurring up to three or four times a week, irrespective of the preparation of insulin used, and frequently required his admission to hospital. During one of these admissions, in 1955, the clinical diagnosis of steatorrhœa was confirmed by fat-balance studies which showed an absorption of 60% of ingested fat; the stool contained, on average, 50 g. of fat and 6·6 g. of nitrogen per day. Radiography of the abdomen showed extensive calcification of the pancreas (fig. 2) and the results of analysis of the duodenal aspirate following the injection of secretin and pancreozymin confirmed the complete absence of exocrine pancreatic function, there being virtually no response in the pH, rate of flow, or bicarbonate, amylase, trypsin, or lipase content. Subsequent treatment with pancreatin materially improved the steatorrhœa but not the nocturnal diarrhœa.

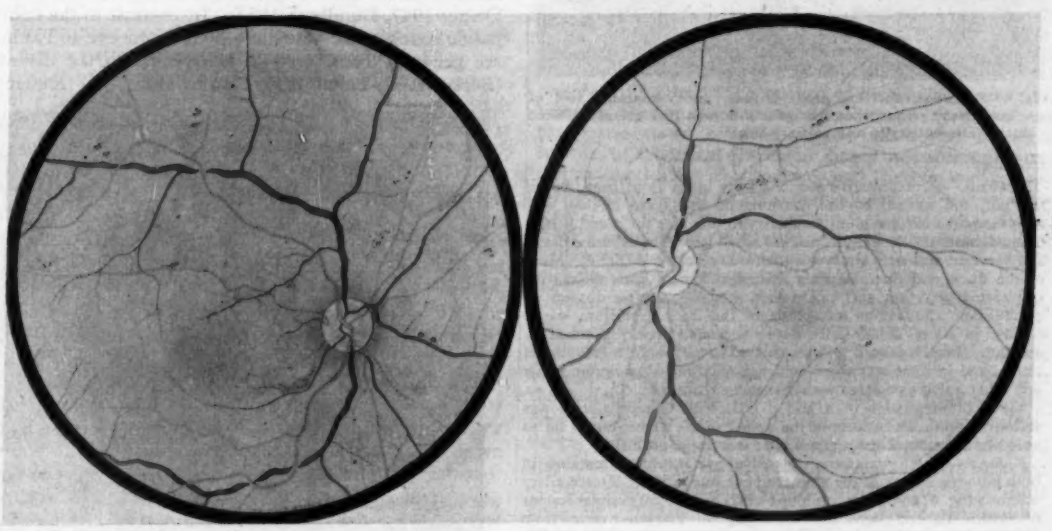
**Fig. 2—Oblique film of abdomen, showing calcification of pancreas.**

There was no family history of diabetes. His parents died in their 70s; none of their parents or siblings had diabetes. He had two elder brothers alive and well; and both they and the patient were of normal weight at birth.

*Necropsy Findings*

The necropsy was carried out two hours after death.

*Pancreas.*—32·2 g. (fig. 3). The organ consisted mainly of fibrous tissue and nodules of calcium; very little true pancreatic tissue could be identified. The main pancreatic duct could not be found from the duodenal aspect, but in the head of the pancreas it could be seen distended by a small white calculus, 0·3 cm. in diameter.



(*a*) (*b*)

**Fig. 1—Drawings of retinæ, showing early diabetic retinopathy—varicosity of some veins, clusters of small micro-aneurysms, round blob hæmorrhages, and discrete exudates. (*a*) right eye: (*b*) left eye.**

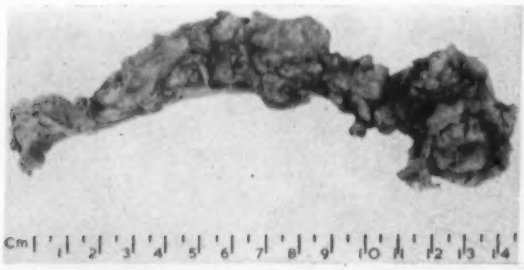


Fig. 3—Pancreas, showing gross calcification.

*Kidneys.*—Right 300 g., left 225 g. Both organs showed moderate hydronephrosis with chronic pyelonephritic scarring, and there were small soft calculi in the left pelvis and calyces. A large perinephric abscess was found in continuity with a small abscess in the upper pole of the right kidney. The perinephric abscess had tracked down the right psoas muscle into the right inguinal region and behind the pubes into the left groin.

*Heart.*—310 g. There was slight left ventricular hypertrophy.

*Coronary arteries and aorta.*—These vessels contained only occasional tiny plaques of atheroma.

*Lungs.*—There was patchy collapse of the right lower lobe.

*Liver and bile-ducts.*—2080 g. The organ was enlarged and congested. The biliary tract was patent.

*Adrenal glands.*—Combined weight 16·7 g. They were both slightly enlarged.

*Pituitary.*—0·55 g. The gland was a little smaller than usual.

No significant abnormalities were found in the other organs.

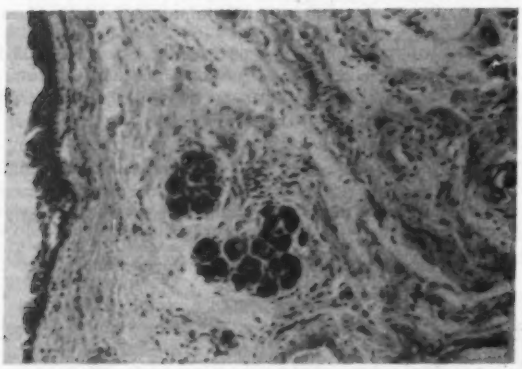


Fig. 4—Pancreas, showing gross fibrosis and remaining foci of acinar tissue. Squamous metaplasia is seen in a greatly dilated duct. (Hæmatoxylin and eosin. ×100.)

*Histology*

*Pancreas.*—Representative sections were taken from head, body, and tail, and stained by the hæmatoxylin and eosin method and with Gomori's chrome alum hæmatoxylin phloxine for α and β islet cells (Gomori 1941). Only occasional small islands of exocrine tissue had survived and were situated in dense fibrous tissue (fig. 4). Most of the ducts and ductules were dilated and many were filled with inspissated secretion and cell debris showing varying degrees of calcification. Squamous metaplasia of the duct epithelium was a feature in many areas. Islet tissue was also greatly reduced in amount. Small localised groups of islets were found in the fibrous tissue, and in none was there evidence of fibrosis, hyalinisation, or any other lesion associated with diabetes mellitus (fig. 5).

Good differentiation of α and β cells with Gomori's stain was technically difficult because of the nature of the tissue, but as far as could be ascertained the α/β cell ratio was not abnormal.

*Kidneys.*—There was fairly extensive pyelonephritic scarring in both kidneys. Many of the glomeruli exhibited diffuse intercapillary sclerosis (fig. 6) and a few contained small but typical nodular lesions of classical diabetic glomerulosclerosis (fig. 7). The latter varied from 20μ to 50μ in diameter. There was moderately severe hyaline arteriolosclerosis.

*Testes.*—Both showed severe atrophy of the seminiferous tubules. No spermatogenesis could be seen, and the tubules, whose basement membranes were considerably thickened, were lined mainly by Sertoli cells. The interstitial cells were increased in number. There were groups of histiocytes containing hæmosiderin in the interstitial tissue but no fibrosis or chronic inflammatory changes were seen.

*Heart.*—Early brown atrophy was present.

*Liver and spleen.*—These organs were congested.

*Lungs.*—There was purulent bronchitis, and collapse in the right lower lobe.

*Parotid glands.*—There were a few foci of fibrosis and lymphocyte infiltration, associated with glandular atrophy, but the glands otherwise appeared normal.

*Adrenal and pituitary glands.*—No histological abnormality.

*Nervous system.*—Complete demyelination and fibrous replacement was found in peripheral nerves from the left leg and in the

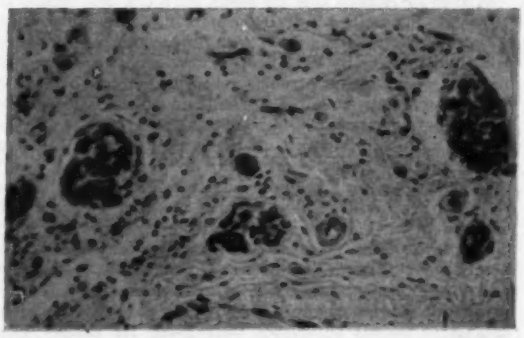


Fig. 5—Pancreas showing a few islets in dense fibrous tissue. (Hæmatoxylin and eosin. ×175.)

"presacral nerve". There was partial demyelination and fibrosis of posterior nerve-roots. No abnormality of the spinal cord or brain could be seen.

## Discussion

The successful therapeutic use of insulin has so reduced the incidence of diabetic coma that very few diabetic patients now die from this cause (Duncan 1951). However, although the life-expectancy of the average patient with diabetes is only a few years shorter than that of the general population (Metropolitan Life Insurance Company 1947), the majority sooner or later develop one or more of the so-called degenerative changes (Mirsky 1946, Dolger 1947, Lundbaek 1954). In contrast to the neuropathic changes, the vascular lesions in the eye and kidney are generally considered to be specific to the disorder (Becker 1952, Leiter 1955, Lukens 1955). So frequently

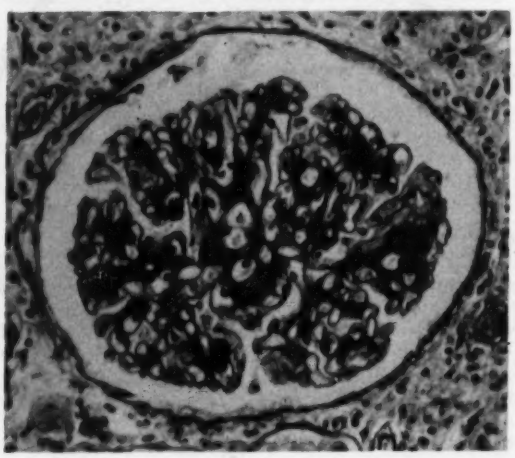


Fig. 6—Glomerulus showing diffuse hyaline sclerosis. (Periodic-acid-Schiff and hæmatoxylin. ×300.)

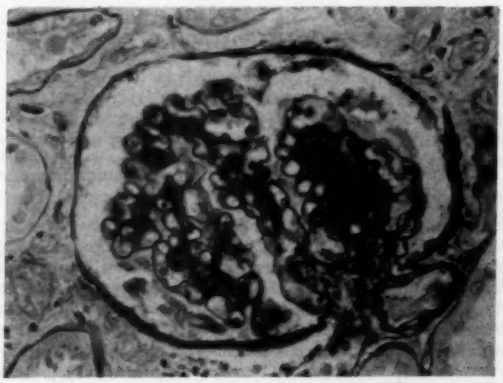


**Fig. 7—Glomerulus showing nodular lesion of classical diabetic glomerulosclerosis. (Periodic-acid-Schiff and hæmatoxylin. ×300.)**

do these changes accompany longstanding and poorly controlled diabetes that some authorities look upon them as an integral part of the disease rather than as complications of it (Dolger 1947, Henderson et al. 1947).

There is little doubt that the predisposition to diabetes mellitus is often inherited, being most probably transmitted as a recessive characteristic, though it manifests itself clinically in only a proportion of those bearing the gene (Steinberg 1955). The tendency to develop the specific vascular changes could similarly be inherited, but the fact that they have not been found with certainty in persons having no demonstrable defect of carbohydrate metabolism (Becker 1952, Mirsky 1952) makes it improbable that they are inherited as an independent diathesis. For the same reason, even if they were transmitted in close association with the diathesis of idiopathic diabetes (Dry and Hines 1941, White and Waskow 1948, LeCompte 1957), their development must depend on the presence of the metabolic disturbance of diabetes, of which the abnormality in carbohydrate metabolism may be only a part.

Reproduction of the lesions of the specific retinopathy or nephropathy in animals made hyperglycæmic by one or other of a variety of techniques would demonstrate that a hereditary basis is not necessarily involved. Such attempts have not been unequivocally successful (Lukens and Dohan 1946, Foglia et al. 1948, Friedenwald 1950, 1952, Mann et al. 1951, Becker 1952, Rickets 1952, Janes and Bounds 1954, LeCompte 1957). Nevertheless, these were short-term experiments, and it may be that the duration, as well as the degree of control, of the diabetes favours the development of these retinal and glomerular changes in man.

Hyperglycæmia, impaired glucose tolerance, and the tendency to develop ketosis can arise in man as the result of disease of the pancreas. The development of the specific retinopathy or nephropathy in such "pancreatic diabetics" would support the view that these complications result from the abnormal metabolism in diabetes rather than as a consequence of an inherited defect. So far as we know, only two such cases have been previously reported.

Sprague (1947) described a patient who developed relapsing pancreatitis at the age of 27 and became diabetic eight years later. After a further nine years he was found to have a specific diabetic retinopathy.

The presence of diabetic retinopathy was recorded by Hudson (1953) in a man, aged 50, suffering from hæmochromatosis who had developed diabetes fifteen years previously.

Three other cases are described in personal communications.

Stawell, in a personal communication to Lawrence (1949), mentions diabetic retinopathy in a patient with diabetes due to hæmochromatosis; Rynearson (1957) describes a patient who developed diabetic retinopathy three years after the onset of diabetes which followed total pancreatectomy; and Dunlop (1957) records the presence of the specific retinopathy in a patient with longstanding diabetes resulting from hæmochromatosis.

The details of Stawell's patient are not known, but in none of the other patients was there a family history of diabetes, and the diabetes was regarded as purely pancreatic in origin.

We believe that the diabetes in our patient was also a true "pancreatic diabetes," there being several clinical features which suggested that his diabetes was due to insulin lack alone rather than to the operation of any anti-insulin mechanisms:

(1) The sensitivity to the blood-glucose-lowering action of insulin (his blood-glucose was noted on several occasions to fall from over 600 mg. to less than 50 mg. per 100 ml. four to six hours after the subcutaneous injection of 12 to 20 units of soluble insulin); this probably accounted for the extraordinary frequency of the hypoglycæmic episodes, even with a moderate daily dose which varied from 28 to 40 units, except when infection necessitated the administration of larger doses. This tendency to hypoglycæmia remained unaltered throughout the entire course of his disorder.

(2) His failure to show any reduction in the concentration of glucose in the blood in response to a dose of 4·5 g. of carbutamide by mouth: the immediate hypoglycæmic effect of carbutamide is believed to be due to the release of insulin from the β-cells of the pancreas, and its absence in this patient suggests that the pancreas was unable to secrete insulin (Houssay and Phenos 1956, Fajans et al. 1956).

(3) The clinical and biochemical evidence of extensive disease of his pancreas was overwhelming. With duodenal intubation no exocrine secretion could be demonstrated in response to stimulation by secretin and pancreozymin, and the stool nitrogen content was elevated. The steatorrhœa thus appears to have been of pancreatic origin. From the patient's observation, pale stools were present eight years after the onset of the diabetes, and this suggests that disease of the pancreas was present at that time. The ætiology of the pancreatic lesion is, however, obscure. Mumps contracted at the age of 11 may have some causal relationship, and the history of vague episodes of abdominal discomfort during adolescence suggests that pancreatitis had already developed. Diabetes may precede the steatorrhœa, and not uncommonly develops within a few years of the first attack of pancreatitis (Maimon et al. 1948).

(4) Finally, the fact that, as far as can be ascertained, none of his known relatives has or had diabetes, is consistent with the view that he had not inherited a diabetic diathesis.

The clinical diagnosis of severe pancreatic insufficiency was confirmed by the finding of gross pancreatic fibrosis at necropsy. The reduction in the amount of islet tissue from the normal appears quite sufficient to account for the patient's diabetic state on the basis of insulin deficiency. The hypothesis that he might have had a coincidental diabetic diathesis is not supported by the histological appearance of the few remaining islets. No hyalinisation or other lesion associated with idiopathic diabetes mellitus could be found, and the proportion of α to β cells seemed to be within normal limits (MacLean and Ogilvie 1955). The appearance of the pancreas was consistent with pancreatitis due to mumps. The presence of the calculus in the main pancreatic duct is probably not of ætiological

significance, since marked calcification was scattered throughout the pancreatic tissue and in most of the ducts.

It was unfortunately not possible to examine histologically the retinopathy visible on clinical examination, but the latter is sufficient to establish its specificity. The presence in the kidneys of typical Kimmelstiel-Wilson bodies was established by the histological examination, though they were few. The diffuse glomerulosclerosis was also thought to be diabetic in nature and to conform to the descriptions by Bell (1953) and Lambie and MacFarlane (1955). It is, however, not as specific to diabetes mellitus as the nodular lesion, since similar changes may be found in type-II glomerulonephritis.

The problem of the relationship between diabetes and the later development of its specific complications will probably remain unsolved until a more intimate knowledge of the biochemical abnormality in diabetes and in the tissues affected by the degenerative changes is available. Nevertheless, the development of these changes in patients whose diabetes appears to be of pancreatic origin is very strong evidence in favour of the view that they are to a large extent the consequence of the metabolic disorder which results from insulin deficiency. Reports of patients similar to our own would be of great value in throwing further light on this problem, which is not merely an academic one. The emphasis commonly placed upon the need for rigid diabetic control will be fully justifiable only if it can be shown that the development of these complications is dependent on or influenced by a derangement of metabolism, and that they are not an inescapable consequence of inheritance.

**Summary**

The precise relationship between the development of the specific vascular complications of diabetes mellitus in the retinæ and of specific nodular glomerulosclerosis to the disorder itself is unknown. A patient has been described in whom both these complications occurred and in whom there was overwhelming evidence to support the view that the diabetes arose as a result of pancreatic disease. The significance of this case in relation to present-day views of the ætiology of these complications is discussed: it constitutes strong evidence in favour of the view that these complications are the consequence of the metabolic disorder which results from insulin deficiency.

For permission to report this case we are grateful to Prof. D. M. Dunlop and Sir Stanley Davidson, in whose charges the patient was investigated. We thank Prof. G. I. Scott and Miss C. Gundry for the ophthalmoscopic examination and drawings, Dr. I. N. Marks who carried out the tests of the pancreatic function, and Mr. T. C. Dodds, of the department of medical photography, for the photographs.

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## TWENTY-NINE CHILDREN WITH SULPHONAMIDE HÆMATURIA

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SHORTLY after the introduction of sulphonamide therapy, hæmaturia was noted as an occasional complication.

The explanation seemed to be that, as urine passes along the renal tubules, it becomes more concentrated and acid, with the result that crystals of sulphonamide may be deposited. The convoluted tubules are first affected (Goodman and Gilman 1955), but deposition of crystals can spread in either direction and give rise to hæmaturia, albuminuria, oliguria, hypertension, or nitrogen retention. Such cases may present with anuria (Atkinson 1957, Browne 1957) or more rarely with obstruction of the urethra (Miller and Mitchell 1952, Rice-Edwards 1950). These happenings may be atributable to overdosage of sulphonamide, inadequate intake of fluid, or the use of a preparation unduly liable to crystallise out at pH values found in the renal tubules.

In the ten years since 1948, a total of 29 patients have been treated in the medical wards of The Royal Hospital for Sick Children, Glasgow, for hæmaturia associated with taking sulphonamide drugs. In all of them:

1. The patient had had sulphonamide therapy before the symptoms began.

2. There were no history or subsequent findings suggestive of renal disease (except those occasioned by sulphonamide crystallisation).

3. Gross hæmaturia and crystalluria were present.

The presence of urinary sulphonamide was confirmed in almost all cases and the serum sulphonamide level estimated in some.

### Clinical Observations

The ages of the 29 children ranged from 1 to 12 years, most being between 1 and 6. Sulphonamide had been given for periods of one to six days in daily doses of 100–400 mg. per kg. body-weight. The blood-pressure was elevated in 14 of the 22 cases in which it was recorded, but it returned to normal levels within a few days. The non-protein-nitrogen content of the blood was raised on 13 of the 21 occasions in which the estimation was made. The hæmaturia lasted one to six days, and albuminuria usually persisted a few days longer.

In 3 cases anuria persisted for more than forty-eight hours; uræmia was present in all three.

**Case 1.**—A girl, aged $6^1/_{12}$, was given sulphamerazine 2 g. daily for two days because of upper respiratory infection. She then complained of loin pain, and developed hæmaturia followed by anuria. After forty-eight hours' anuria her blood-

DR. DUNCAN AND OTHERS: REFERENCES—*continued*

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pressure rose to 148/110 mm. Hg, and she had severe convulsions—probably due to hypertensive encephalopathy. The blood non-protein nitrogen was 125 mg. per 100 ml.

Lumbar puncture, venesection, sedation with phenobarbitone, and hypertonic solutions intravenously were employed before her convulsions ceased. She was given sodium bicarbonate gr. 180 daily, and diuresis began shortly after this was started. Within fourteen days she was symptom-free.

**Case 2.**—A boy, aged 2, was given four doses of sulphamerazine, each 0·5 g. orally, as treatment for a sore throat. He vomited, and developed hæmaturia and anuria. Anuria persisted for seventy-two hours, during which time the blood non-protein-nitrogen rose to 140 mg. per 100 ml. and the blood-pressure to 114/80, and he became fevered. Sodium bicarbonate gr. 180 daily was given and fluid intake restricted to 1 litre daily. Diuresis began and he became symptom-free ten days later.

**Case 3.**—A girl, aged 2, was given 2·5 g. of sulphamerazine daily for four days for a respiratory infection. She then passed " grains of sand " per urethram, and stopped passing urine. Sixty hours later she was admitted to hospital; the urethra was cleared and she voided urine. Treatment was begun with sodium bicarbonate gr. 180 daily. She had anuria for a further forty-eight hours, during which time she was restless and anorexic, and her blood-urea rose to 147 mg. per 100 ml. Her blood-pressure was 150/70; her serum-sodium level had fallen to 114 mEq. per litre and serum-potassium to 3·8 mEq. Supplementary potassium was added to her intake of 250 ml. of 25% glucose solution daily, and diuresis began after five days of anuria. This urine contained erythrocytes and sulphonamide and her serum-sulphamerazine content was 13·8 mg. per 100 ml., more than a hundred hours after oral therapy had stopped.

As the following table shows, 27 of these 29 children had been given a preparation containing sulphamerazine.

| Drug | No. of cases | Dosage mg. per kg. per day |
|---|---|---|
| Sulphamerazine .. .. .. .. | 26 | 100–400 |
| Sulphasomidine .. .. .. .. | 1 | 200 |
| Sulphadimidine .. .. .. .. | 1 | ? |
| Triple sulphonamide * .. .. .. | 1 | 210 |

* A mixture of sulphamerazine, sulphathiazole, and sulphadiazine.

One specific brand of aqueous suspension was prescribed for 22 of these 27 cases. In 13 the dose of sulphamerazine had been 100–200 mg. per kg. per day; in 7 it had been 200–400 mg. per kg. per day, and in the remainder indeterminate.

Our treatment in these cases was essentially conservative. Administration of sulphonamide was stopped, and, where excretion of urine was adequate, copious fluids were given together with sodium bicarbonate gr. 30 four-hourly. When anuria and uræmia arose, fluid intake was restricted and glucose administered. Hypertensive encephalopathy was treated by sedation, lumbar puncture, and venesection.

This cautious approach to treatment seems justified in that all cases to date have recovered completely.

### Discussion

The dosage of 'Cremomerazine' recommended by the manufacturers for the first four years of life amounts to about 110–220 mg. per kg. for the first day and about 70–140 mg. per kg. per day thereafter (dosage refers to sulphamerazine content). It is disturbing to find that 13 of the present patients were receiving doses which approximated to such levels of dosage, though in most cases the drug had been given more frequently than twelve-hourly. 1 boy had received only 2 g. (190 mg. per kg.) when anuria began. There is no evidence that the fluid intake of these children was restricted. It may be true that, under ideal conditions, with twelve-hourly doses and copious fluid and alkali administration, sulphamerazine seldom produces hæmaturia, but the overriding consideration here is that in actual practice this drug may cause hæmaturia, azotæmia, and hypertension in children when given at a dosage level in frequent use. To justify giving a drug potentially noxious in therapeutic doses one must show that it has significant advantages over other preparations. Sulphamerazine seems to me to have no outstanding virtue which would lead me ever to prescribe it.

Many cases of sulphamerazine hæmaturia have been reported (Sheppard 1948, Atkinson 1951, Brand 1951, Rendle-Short 1951, Morton and Dobbs 1951), but probably many more cases with slight hæmaturia have not been recognised. There is a risk that hæmaturia following the treatment of upper respiratory infections with sulphamerazine might simulate acute hæmorrhagic nephritis and so mislead the clinician.

### Summary

29 cases of hæmaturia following administration of sulphonamide drugs are recorded. Anuria, hypertension, encephalopathy, and uræmia were seen in some patients, but all subsequently recovered.

27 of these patients had been given sulphamerazine, and in many cases the dose was not excessive as judged by one manufacturer's recommendations. It seems doubtful whether the use of this drug is justified.

I should like to thank Prof. Stanley G. Graham and Dr. J. H. Hutchison for allowing me to use their case-records.

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## METHOD OF ESTIMATING THE DIAMETER OF ERYTHROCYTES

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THE diameter of the erythrocytes can be measured by many methods, most of which are rather laborious and require special equipment. A fairly simple method, requiring no special equipment, is to spread a blood film from a normal control on top of a stained film with the erythrocytes to be measured, and then to compare the relative sizes of stained and unstained erythrocytes. This method has for many years been occasionally used in Norway, and undoubtedly in many other countries. Bessis (1956) mentions the method, giving Pittaluga the credit for introducing the method to him.

This method of superimposed blood films has, however, certain drawbacks: it is difficult to make both films thin enough in the same places to avoid overlapping of stained and unstained erythrocytes; the stained film is often scratched when the superimposed unstained film is being spread; and the process of staining might change the

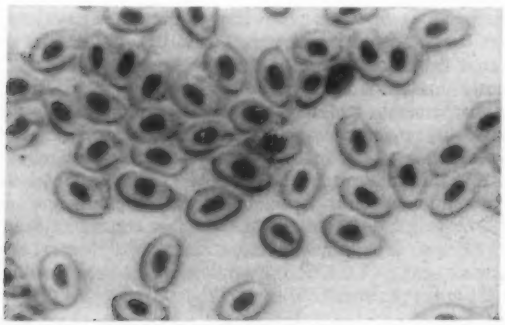

Fig. 1—Hens' erythrocytes.

size of the erythrocytes—but this change in size is usually surprisingly small.

All these difficulties would be avoided if one could mix blood from the unknown and the control before spreading the film and still be able to decide which erythrocytes in the film belonged to the unknown and which to the normal control. Erythrocytes of birds are elliptical and contain a nucleus—features which clearly distinguish them from human erythrocytes. We have

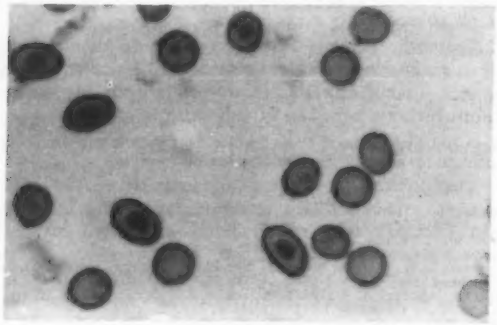

Fig. 2—Mixture of normal human and hens' erythrocytes.

lately made films from a mixture of hens' blood and human blood and have estimated the size of the human erythrocytes by comparing them with the hens' erythrocytes.

Heparinised blood is collected from a killed hen and may be kept in the refrigerator for days or weeks until needed. Two drops of hens' blood is added to 0·5 ml. of heparinised or oxalated human blood, and a film is made

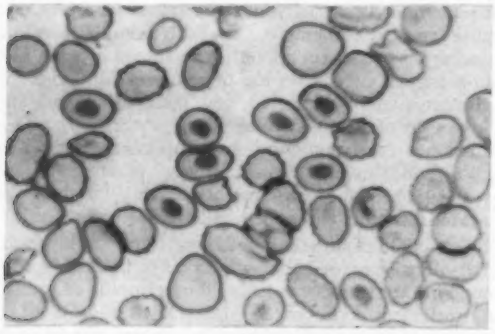

Fig. 3—Mixture of human erythrocytes from a patient with pernicious anæmia and of hens' erythrocytes.

from the mixture and stained with Wright or Giemsa stain. Hens' erythrocytes are elliptical, with a longitudinal diameter of about 11·0 μ and a lateral diameter of 6·7μ (90% of hens' erythrocytes have a longitudinal diameter between 9·8μ and 12·2μ, and 90% have a lateral diameter between 5·8μ and 7·6μ). The size of a particular hen's erythrocytes is checked against a normal human control before the hen's blood is used for estimating the size of human erythrocytes.

If one does not want to keep a supply of hens' blood in the refrigerator, two drops of blood is easily obtained from a cut in a hen's comb.

Fig. 1 shows a stained film of hens' blood, fig. 2 a film made from a mixture of hens' blood and normal human blood, and fig. 3 a film from a mixture of hens' blood and blood from a patient with untreated pernicious anæmia.

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## ONE RADIOGRAPH TO EXCLUDE PLACENTA PRÆVIA

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PLACENTA prævia may present as either antepartum hæmorrhage or (without antepartum hæmorrhage) as malpresentation, unstable position, or a high fœtal head. The modern management of placenta prævia has drastically reduced maternal and fœtal mortality (see table).

Expectant treatment (Macafee 1945, 1946, Johnson 1945, 1950, Grant 1955) aims to continue the pregnancy into the 37th week, when the fœtus has every chance of surviving. The patient has to be admitted for 1–6 weeks before a low implantation of the placenta can be excluded or confirmed. Under anæsthesia the lower uterine segment is examined digitally through the cervix. If the placenta is then detected anterior to but not beyond the internal os of the uterus, the membranes are ruptured; but if it is palpable in any other position, immediate lower-segment cæsarean section is the treatment of choice. If the placenta is not palpable, the pregnancy may be allowed to terminate spontaneously.

Our object was to find a reliable simple diagnostic method, so that those patients who were conclusively found not to have a placenta prævia could be spared a long stay in hospital. We wished to avoid both unnecessary filling of valuable hospital beds and the emotional strain experienced by many mothers because of enforced absence from their homes and families, as well as the taking of numerous radiographs for localising the placenta; this may be dangerous because of irradiation of the fœtus (Stewart et al. 1956) and the mother (Medical Research Council 1956), and is expensive in film and the time of highly skilled staff.

We have investigated the accuracy and practical value of a single lateral radiograph of the uterus in cases of suspected placenta prævia.

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## Material and Methods

107 patients were investigated between January, 1953, and June, 1956. The position of the placenta was estimated radiographically *only* if the information would help in the clinical diagnosis. Antepartum hæmorrhage, malpresentation, unstable lie, or high fœtal head were the indications for radiography.

The apparatus consisted of a standard four-valve X-ray unit with a rotating anode tube and tilting table.

Three radiographs were taken routinely in each patient. These were lateral views of the uterus, the pelvis in the erect position, and the pelvis in the semi-erect position.

The films were read on a standard viewing-box. Separate illumination by a 100-watt bulb was necessary for viewing the anterior aspect of the uterus and adjacent abdominal wall. A wedge filter was not used while taking the radiographs.

Various radiographic techniques have been developed to find the position of the placenta. Soft-tissue radiography (direct placentography) has proved the most valuable (Snow and Powell 1934, Dippel and Brown 1940, Bishop 1945, Reid 1949, 1951, 1953, Stallworthy 1950, 1951, Murray 1953, Hartley 1954, Dawson and Mitchell 1954). Further information is obtained by radiographic measurement of the displacement of the fœtal head from the sacral promontory and symphysis pubis at the pelvic brim (indirect placentography) (Ball and Golden 1941, McCort et al. 1944, Bishop 1945, Reid 1951).

Cystography (Ude et al. 1934, Dippel and Brown 1940) is not generally used now because it is unreliable.

Amniography (Menees et al. 1930, Kerr and McKay 1939, Savignac 1953, Williams 1956), aortography (Hartnett 1948), retrograde femoral arteriography (Sutton 1952), and localisation of the placenta by radioactive sodium (Browne 1951) are experimental techniques.

Both direct and indirect placentography were used during this investigation. As a precaution, the patient was asked to empty her bladder and rectum before being radiographed.

## Results

The placenta was correctly identified in the upper uterine segment in 90 of the 107 cases. At the beginning of the investigation the placenta in 1 of the 107 cases was wrongly interpreted as entirely in the upper segment; examination under anæsthesia revealed a second-degree anterior placenta prævia.

Using soft-tissue and displacement radiographic techniques, placenta prævia was missed in 3 cases, and correctly diagnosed in 12 cases; the radiographic findings were inconclusive in 2 cases. It was observed that, if there was no placental shadow in the upper uterine segment, placenta prævia was likely to be found clinically. In practice, these patients must be admitted; most have placenta prævia.

Of the 90 cases in which the placenta was correctly identified in the upper uterine segment, 54 were associated with antepartum hæmorrhage. The causes of antepartum hæmorrhage were analysed as follows:

| | | | |
|---|---|---|---|
| No cause found | 30 | Erosion of cervix * | 3 |
| Abruptio placentæ | 16 | Varicosities of cervix | 1 |
| Circumvallate placentæ | 3 | Polyp of cervix | 1 |

* 1 case proved to be invasive carcinoma of the cervix.

## Discussion

The most significant conclusion reached was that radiological evidence of the placenta in the upper uterine segment is highly accurate; a lateral radiograph of the uterus taken after 34 weeks' gestation, in the absence of hydramnios, yielded the necessary information to exclude placenta prævia. It was found that the management of 90 out of the 107 patients investigated could have been decided with accuracy on the evidence of single lateral radiograph of the uterus.

MORTALITY-RATES IN PLACENTA PRÆVIA

| Treatment | Series | Maternal mortality (%) | Fœtal mortality (%) |
|---|---|---|---|
| Active (pre-modern) | Berkeley (1936) | 7·0 | 59·0 |
| | Browne (1939) | 5·9 | 54·0 |
| Modern with expectant | Macafee (1945) | 0·57 | 23·5 |
| | Grant (1955) | 0·00 | 9·9 |

Therefore, we felt it was safe to allow the patient to go home from hospital when placenta prævia had been excluded radiographically. In a woman who has had antepartum hæmorrhage, the os should be inspected through a speculum after a week's rest, to exclude lesions of the cervix; she is then allowed to return home. We have latterly adopted this procedure without regrets. Chassar Moir (1956) supports this view:

> " If in a case of antepartum hæmorrhage a low implantation of the placenta can be excluded, the patient can be spared the necessity of a vaginal examination, and can, after a week's rest, be allowed to return home without fear of renewed, violent hæmorrhage."

## Summary

Radiographic evidence of the placenta in the upper uterine segment is highly accurate. A single lateral radiograph of the uterus after 34 weeks' gestation is enough to exclude placenta prævia.

Of 107 patients investigated by direct and indirect placentography (soft-tissue radiographs and measurement of the displacement of the fœtal head), 17 had placenta prævia, which was diagnosed correctly in 12 cases and suspected in 2.

A lateral uterine radiograph requires no special skill or equipment, but transillumination of the film by a 100-watt bulb may be needed to detect the anterior wall of the uterus and the abdomen. One such radiograph is compatible with good obstetric standards; irradiation to the fœtus and mother is minimal; film costs are reduced; and fœtal abnormalities may also be detected.

X-ray location of the placenta in the upper uterine segment relieves the patient's anxieties for she can be sent home without fear of violent hæmorrhage, and hospital beds are not filled unnecessarily.

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# Preliminary Communications

## NUCLEAR CHANGES IN ORAL EPITHELIUM IN PERNICIOUS ANÆMIA

EPITHELIAL atrophy of the tongue is said to occur in about 70% of cases of pernicious anæmia,[1] but little study has been made of the response of the tongue to specific treatment. An attempt was therefore made to examine cytological material from the tongue, but preparations were unsatisfactory, probably because of the heavy keratinisation of the epithelium. Examination of oral mucosa from the inside of the cheek has, however, proved more satisfactory and a study of nuclear abnormalities and changes in size has been made in patients with pernicious anæmia.

Changes in gastric columnar cells in pernicious anæmia have been reported by Massey and Rubin,[2] while desquamated squamous cells present in gastric aspirate were examined by Graham and Rheault.[3] They measured the greatest cytoplasmic diameter and found it increased. Recently Boen [4] has described nuclear changes in exfoliated squamous cells from the mouth and has made comparative measurements of the longer axis of the nucleus. In seven out of his ten patients with pernicious anæmia, enlarged squamous-cell nuclei were seen and the nuclei were restored towards normality by specific treatment. The three cases with relatively normal nuclei were excluded from this comparison. Morphological abnormalities of the nucleus, and in particular a reticulated chromatin structure, were found to disappear during treatment. A series of normal controls matched according to age were also examined by Boen.

In the present study, preparations of oral mucosa have been taken by scraping the inside of the cheek with a microscope slide. Thirty-nine cases of pernicious anæmia have been studied in this way and similar changes of nuclear size and morphology noted. Twenty-five of these cases have been re-examined later at periods varying from 2 to 32 months from the date when they were first diagnosed and treated, and in twenty-two of these there has been evidence of diminution in nuclear size. In all cases 100 nuclei have been measured in both longer and shorter axes, and the averages of these measurements used for comparison.

Material from ninety-five normal controls of varying ages has also been examined by the same technique. By relating nuclear size to age (see figure), a surprising increase of the shorter axes of the nuclei becomes evident. The effect is obvious only over the age of 60, and if normal controls of 60 years and over be compared with the rest a significant difference arises ($P<0.05$). For this reason, the results from cases of pernicious anæmia have been compared for each axis within two age-groups—35–59 years, and 60 years and over.

TABLE I.—MEAN AXIS MEASUREMENTS IN PERNICIOUS ANÆMIA AND CONTROLS

| Cases | Age range | No. | Mean and standard error | | Standard deviation | |
|---|---|---|---|---|---|---|
| | | | Longer axis | Shorter axis | Longer axis | Shorter axis |
| Pernicious anæmia | 35–59 | 17 | 12·127 ± ·293 | 9·496 ± ·231 | ±1·210 | ±0·953 |
| | 60+ | 22 | 12·342 ± ·202 | 9·618 ± ·203 | ±0·945 | ±0·950 |
| Normal controls | < 35 | 33 | 11·709 ± ·117 | 8·435 ± ·127 | ±0·670 | ±0·728 |
| | 35–59 | 41 | 11·636 ± ·091 | 8·558 ± ·108 | ±0·582 | ±0·694 |
| | 60+ | 21 | 11·920 ± ·112 | 8·930 ± ·123 | ±0·512 | ±0·561 |

TABLE II—PERNICIOUS ANÆMIA AND CONTROLS : ANALYSIS OF RESULTS

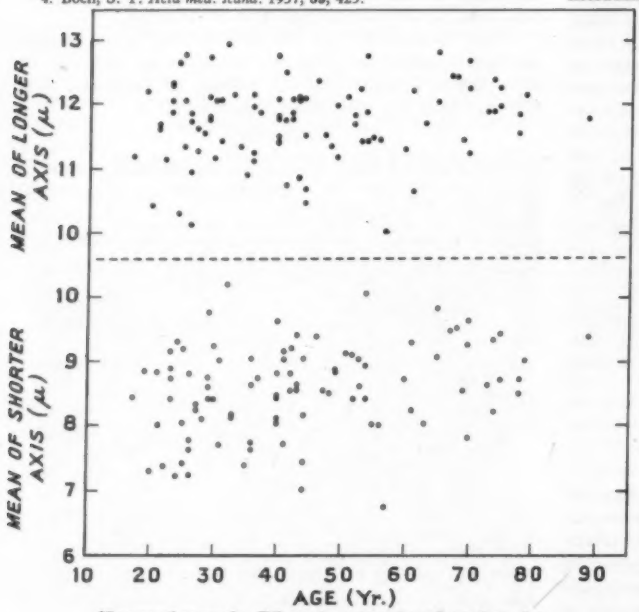
| Age range | t | | P | |
|---|---|---|---|---|
| | Longer axis | Shorter axis | Longer axis | Shorter axis |
| 35–59 | 1·60 | 3·68 | not signif. | < 0·001 |
| 60+ | 1·83 | 2·91 | not signif. | < 0·01 |

When all thirty-nine cases of pernicious anæmia, including those few with relatively normal nuclear size, are compared with their controls in the two age-groups, it becomes apparent that measurements in both axes in pernicious anæmia are greater than in controls (table I). This apparent increase in size in the pernicious anæmia nuclei falls just short of significance level for the longer axis, but is highly significant for the shorter (table II). The degree of significance is less for the over-60 age-group and this appears to be due to the effect of age upon the normal controls.

Ten cases of normocytic normochromic anæmia have also been examined and the nuclear size has been found to lie within the normal range. Groups of controls with achlorhydria and oral sepsis show no significant departure from the normal.

One patient with a smooth tongue in the absence of anæmia, with a normal level of serum-iron, and with free acid in the stomach was found to have abnormally large squamous-cell nuclei which reverted towards normal with oral administration of vitamin-B complex. Results in iron deficiency are being studied.

One may conclude therefore that squamous-cell nuclei from the mouth are abnormally large, particularly in the shorter axis, in pernicious anæmia, and that they revert

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towards normal with treatment. In the elderly the nuclei tend to be larger. It appears that megaloblastic anæmia may not be the only condition in which abnormally large nuclei are seen.

I should like to thank Prof. C. B. Perry, Dr. W. A. Gillespie, and Dr. F. G. Bolton for much advice and encouragement, and Miss E. H. L. Duncan for statistical help. The work is being done with the aid of a grant from the governors of the United Bristol Hospitals.

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## CLINICAL DEXTRAN FOR ACUTE EPISODES IN PAROXYSMAL NOCTURNAL HÆMOGLOBINURIA

IN 1955, Pillemer [1] described properdin as a natural immune property of serum, and later Hinz et al.[2] brought forward evidence that the hæmolysis of the red blood-cells in paroxysmal nocturnal hæmoglobinuria was due to the interaction of properdin with the stroma of the intact red cells.

One of us (F. S.) found that, in some healthy persons of blood-group O, the properdin titre differed according to the temperature at which the red cells are separated from the serum. In these people, if whole defibrinated blood was used and the mixture allowed to stand at 0°C for $1^1/_2$ hours, the properdin titre was altered, and in some cases a much lower titre was obtained than when the serum was separated from the blood at 37°C immediately after it had been collected. If, before the whole defibrinated blood was cooled to 0°C, certain substances, including clinical dextran, were added in suitable concentration, the subsequent cooling of the mixture to 0°C did not decrease the properdin titre.

Dextran was, to some extent, anticomplementary and was also one of several substances which, in certain concentrations, prevented the activity, in most cases, of any previously existing cold incomplete anti-H antibody. There are many explanations of the interference with the properdin content of the serum associated with the incubation of group-O blood with its own cells at 0°C in these cases; one is the possibility that it is associated with the union of cold incomplete anti-H antibody with the red cells at this temperature. This relationship is being worked out, and further details will be published later.

These laboratory investigations suggested that clinical dextran might be valuable for the control of the acute episodes of paroxysmal nocturnal hæmoglobinuria; so it was tried in two cases.

**Case 1.**—A man with typical paroxysmal nocturnal hæmoglobinuria had been under observation in the department of hæmatology for $2^1/_2$ years and occasionally had to be admitted because of acute episodes of hæmoglobinuria that sharply lowered his hæmoglobin level. Such episodes were usually treated by blood-transfusions, but in one of them infusions of clinical dextran were substituted for blood-transfusion. The dextran infusions were effective, and the hæmoglobinuria ceased; but it recurred some time after the dextran infusion had stopped.

**Case 2.**—A married woman with typical paroxysmal nocturnal hæmoglobinuria was under the care of Dr. M. L. Thomson of Salford Royal Hospital. She had been under observation for many years, and the present attack of hæmoglobinuria had lasted 6 weeks. She was admitted to hospital, and her hæmoglobin was 7·5 g. per 100 ml. Clinical dextran 1 litre was infused, and next morning her urine contained no hæmoglobin. Next day she had a transfusion of packed washed cells, which was followed by pyrexia and a rigor; and some hæmoglobinuria returned, with failure of the hæmoglobin to increase by the expected amount. On the day after the transfusion the patient was infused with clinical dextran 500 ml., and this was followed by considerable diminution in the hæmoglobinuria, which in two or three days disappeared altogether. Her hæmoglobin on leaving the hospital was 8 g. per 100 ml. When she attended the outpatient department ten days later, her hæmoglobin was 9·5 g. per 100 ml., and there had been no recurrence of hæmoglobinuria.

It is, of course, well known that hæmoglobinuria developing in paroxysmal nocturnal hæmoglobinuria will sometimes stop spontaneously. The results we have obtained are suggestive, but it is clear that the treatment could be tried on more patients. Since individual physicians rarely see more than one or two cases, we are publishing this report at an early stage in the hope that others will be interested in trying the infusion of dextran during an acute episode of paroxysmal nocturnal hæmoglobinuria.

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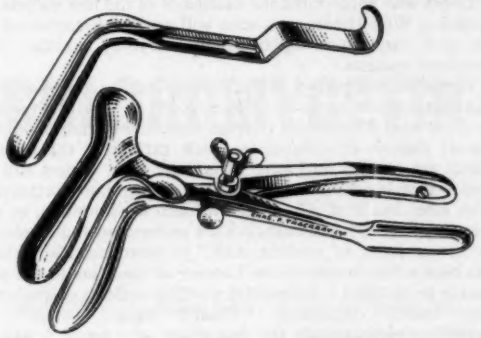
# New Inventions

## THREE-BLADED SPECULUM FOR INTERNAL ANAL SPHINCTEROTOMY

THE treatment of chronic anal fissures by deliberate division of the internal sphincter is the method favoured by an increasing number of surgeons. For its accurate performance a speculum is required which separates the anal margins and exposes the posterior wall of the anal canal for incision. Some variety of bivalve speculum is commonly used for this purpose, but in my experience this has not always given entirely satisfactory access, and I have recently designed a three-bladed speculum which I think has certain advantages (see figure).

The instrument has two main lateral blades, to each of which a handle is attached at one end almost at right-angles to the axis of the blade. The two handles are connected at a pivot $1^1/_8$ inches from the blades. Normally the two handles are kept apart by a spring which brings the blades of the instrument into firm apposition. The coopted blades form a smooth and more or less cylindrical mass of metal which has a conical tip like a fairly narrow tubular proctoscope and



is easily introduced into the anal canal. Once the speculum is in position with its handles lying anteriorly, the blades are separated by approximating the handles gradually against the resistance of the spring. When the required degree of separation has been achieved it can be maintained by tightening a distraction screw.

In many cases this manœuvre by itself gives an excellent view of the posterior anal wall, sufficient for sphincterotomy. In some patients, however, internal hæmorrhoids are present in addition to the fissure, and the right anterior pile tends to bulge into the lumen between the front edges of the lateral blades. To overcome this difficulty a third (anterior) blade has been devised to retract this wall strongly forwards. It is attached by a handle to the pivot of the speculum, and when in place it always provides untrammelled access to the posterior wall and its fissure.

Another feature of this speculum is that each of its three blades is slightly waisted near its external end. When the expanded instrument is in situ, the anal sphincters grip this waist so that, by downward traction in an axial direction, the surgeon can to some extent draw the internal sphincter out of the anal canal and render its distal portion specially prominent for division.

Though this speculum was designed primarily for internal sphincterotomy, it also affords ideal exposure for other fairly common operations—e.g., removal of hypertrophied anal papillæ under local anæsthesia in the outpatient department, and for diathermy of benign tumours of the extreme lower end of the rectum. It is also admirable for submucosal hæmorrhoidectomy according to the technique advocated by Parks.[1]

The speculum was made to my specification by Messrs. Charles F. Thackray, of Leeds.

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# Reviews of Books

## The Extra Pharmacopœia

24th ed. Vol. I. London: Pharmaceutical Press. 1958. Pp. 1695. £3 5*s*.

IT is seventy-five years since the first edition of Dr. Martindale's *Extra Pharmacopœia* appeared; and the fact that it is now in its 24th edition testifies to the esteem in which it is held the world over. The many new remedies introduced in the past six years have made the new edition much bulkier than any of its predecessors. Because "Martindale" is a book of reference and not a textbook, information about older drugs, even though now seldom used, must be retained. Some sections have indeed been pruned; but the omissions are few compared with the additions. The main titles of drugs are now in English instead of Latin—a change that conforms with the practice now followed in the *B.P.* and *B.P.C.* It is perhaps unfortunate—yet unavoidable—that most of the text was compiled with reference to the 1953 *B.P.* and 1955 *Addendum*, but a section on the changes brought about by the *B.P. 1958* is included at the beginning of the book. It is pleasing to note that the abstracts of original papers, which are such a feature of "Martindale", are now more critically selected; and this also applies to the therapeutic index, which no longer includes many references of historical interest only. The special section on antibiotics introduced in the last edition has been expanded, and there is a valuable new section on radioactive isotopes.

The text is as up to date as can be, and the editors and their collaborators are to be congratulated on a large task ably fulfilled.

## Atlas of Systematic Human Anatomy

Vol. III. GERHARD WOLF-HEIDEGGER, M.D., PH.D., professor of anatomy and prosector at the Anatomical Institute of the University of Basle. Edinburgh and London: E. & S. Livingstone. 1957. Pp. 167. 55*s*.

THOSE who appreciated the excellence of the first volume of Professor Wolf-Heidegger's atlas will not be disappointed in the new one, which illustrates the nervous, vascular, and lymphatic systems.

Foreword and preface are in English; the section headings and title captions are in German, which is no real disadvantage to those who do not read German since the reading matter is almost entirely distributed in labels explaining the figures, which are couched in Latin. No doubt some readers will be able to translate these terms into English anatomical vernacular with ease; but Prof. G. A. G. Mitchell's assumption, in the foreword, that "Latin terms . . . are understood and employed by the majority of medical men" is overoptimistic. There has been a big decline in the Latinity of medicine in the past decade or two, and it is doubtful whether students or graduates who cannot distinguish "ilium" from "ileum", or appreciate philologically the desirability of "dorsal", will be able to disentangle the nominatives and genitives of "confluens sinuum" or "R. radicularis r. spinalis a. vertebralis". The section on the brain is excellent, and the draughtsmanship of the figures illustrating vessels and lymphatics is of the highest order, though many of them seem overburdened with details and labels.

Just how useful are such atlases, however excellent in execution? Most professional anatomists would be at once attracted by this volume, and perhaps it should be in their departments. But such atlases are too expensive for students or graduates preparing for higher qualifications; and anyway both would be better advised, like their clinical elders, to learn or revise by direct experience of living or cadaveric structure. The draughtsmanship, the scholarship, the printing, are, as in some other atlases, superb; but is the effort justified?

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**Forensic Medicine** (London: Edward Arnold. 1958. Pp. 340. 30*s*.).—The medical student usually prefers a short textbook, and here he is lucky, for Dr. Keith Simpson's is not only short but one of the most readable and informative of all books designed for medical students. We have no hesitation in recommending it. Many of the changes in the new edition have been made necessary by new laws and regulations or recently discovered drugs for which "the doctor must be on the *qui vive*—or rather *qui mort*". There are several new illustrations of good quality, but many of the familiar ones remain.

**Recent Advances in Obstetrics and Gynæcology** (9th ed. London: J. & A. Churchill. 1958. Pp. 348. 38*s*.).—A new edition of Mr. Aleck Bourne and Mr. Leslie Williams' book appears every five years or so, and each is probably more valuable and popular than its predecessors. The authors have by now, so to speak, got into their stride. They try not to record indiscriminately all the latest discoveries, but rather to present a summary, and accompanying criticism, of consolidated advances. They succeed admirably. The new volume includes chapters on acute renal failure, anæmia in pregnancy (by L. Steingold), coagulation defects, and intravascular thrombosis; and all are very good. Purely clinical are those dealing with the present knowledge of uterine cancer and that entitled Changing Trends in Obstetrics, in which is to be found a faint hint of things to come. Under antenatal care are considered anæmia, diabetes, abnormal weight gain, and the dangers of radiology—no mention of the mechanistic troubles that occupied so prominent a place in the past. Perhaps in a future edition the whole chapter on antenatal care will be concerned with the importance of securing and maintaining the health of the pregnant woman. The authors are so broad-minded as to present all sides of any debatable subject and so experienced as to be dogmatic when dogma is desirable. The book is well illustrated and so delightfully written that the authors must plainly have enjoyed their task. This excellent production is probably the best of the series.

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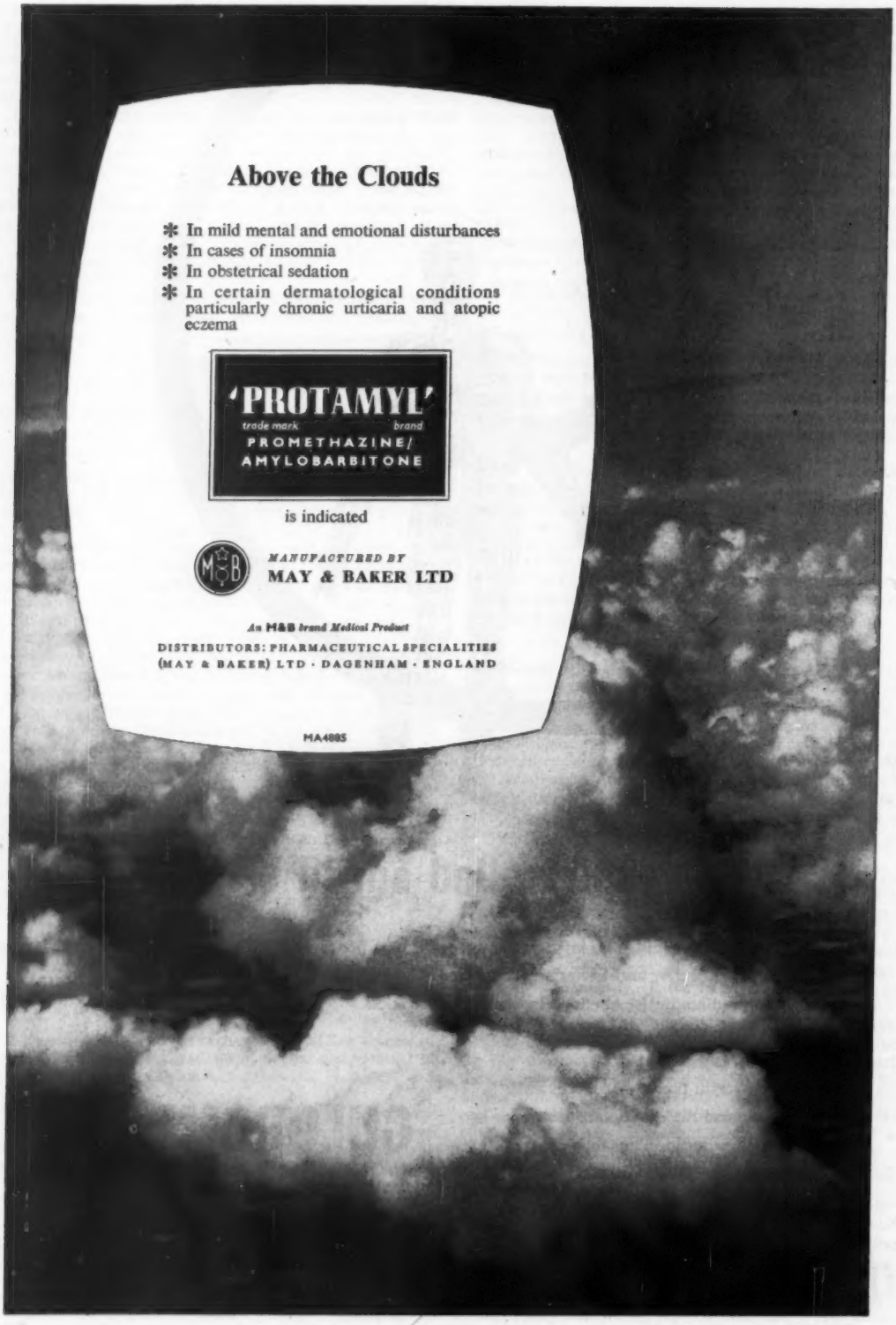
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## Influenza 1889 and 1957

IT is nearly a year since the influenza epidemic which began in China reached Hong Kong and Singapore. From the beginning this epidemic aroused more than ordinary public interest, because of the predictions (accurate in the event) that the Asian virus would spread throughout the world, and because of the rush to prepare vaccine with the new virus in advance of the epidemic wave. But there was another reason for public interest and for some disquiet. In the minds of many people epidemic influenza is forever associated with the pandemic of 1918–19, when influenza is estimated to have caused nearly 20 million deaths, and echoes of this were awakened by a series of most unusual laboratory findings.

Very early in the epidemic MEYER et al.[1] showed that sera taken from people before the epidemic reached the U.S.A. were virtually devoid of antibodies to the Asian virus. This finding was an important factor in predicting a high incidence of influenza in the autumn of 1957, and it also allowed the conclusion that viruses like the Asian virus were newcomers to the population. Shortly afterwards, however, MULDER[2] reported briefly that some of the people in Holland aged 80–90 had small amounts of antibody to the Asian virus. Since antibody was known to be rare or absent in younger people, MULDER suggested that the antibody in these old people might have resulted from infection during their childhood with a virus closely related to the Asian virus. These childhood infections could have corresponded in time with the world-wide influenza epidemic of 1889; which suggests a most interesting hypothesis —that after the 1889 epidemic the virus remained dormant, possibly in an animal reservoir, until it reappeared in 1957. This week we publish three important papers describing evidence for and against this hypothesis. The arguments are to some extent concerned with technical laboratory findings, but this is not just an academic problem. If MULDER's hypothesis is correct we have to ask ourselves what has happened to the virus of the 1918–19 pandemic. Will it, too, reappear, and if so will it be as virulent as before?

Professor MULDER and Dr. MASUREL (p. 810) describe the laboratory findings concerning antibodies to the Asian virus and outline the hypothesis concerning the relation to the 1889 epidemic. As a first step sera were collected from people of different ages in Holland before signs of epidemic spread of the virus had appeared, and through the World Health Organisation other laboratories were asked to collaborate in this investigation. The sera were examined individually for antibody to Asian virus by the hæmagglutination-inhibition test, the sera being pre-treated with a filtrate of *Vibrio choleræ* to remove normal inhibitors of agglutination. Positive hæmagglutination-inhibition titres were found in 52 of 1256 sera examined. The proportion of positive titres increased with age, being in the range 1–2% in the 30–69 age-group, 5% in the 70–79 group, and 22% in the 80–89 group. The same sera showed antibody by an independent test (the mouse-protection test), and there is little doubt that both tests were measuring true antibody. The results of complement-fixation tests with the same sera make it clear that the antibody had not resulted from recent infection with Asian viruses. The problem then is: what is the significance of the antibody and of its age-distribution? MULDER and MASUREL conclude that the human race was in contact with the dominant hæmagglutinating antigen of the Asian virus in the last quarter of the 19th century, and that the 1957 epidemic probably represents a repetition of the 1889 epidemic. We are reminded that the 1889 epidemic probably originated in Central Asia and perhaps in China. Their conclusion is based, however, on the age-distribution of the antibody and on the evidence of DAVENPORT et al.[3] that, generally speaking, the age-distribution of the serum antibodies to different antigenic varieties of influenza virus reflects the prevailing viruses during the childhood of the people of the different age-groups. Thus MULDER and MASUREL draw an analogy between antibodies to the Asian and swine influenza viruses; there is good evidence that the latter were prevalent at the time of the 1918–19 epidemic.[3–5] The conclusions of MULDER and MASUREL are supported by DAVENPORT,[6] who found that in Michigan, U.S.A., antibody detectable by complement-fixation with Asian-virus antigen was not present in persons below the age of 30, but was usually present at low levels in those over 30.

The other side of the argument is set out by Dr. CLARKE and her colleagues (p. 814). They found that of 154 sera collected in England before July, 1957, only 6 gave hæmagglutination-inhibiting antibody to the Asian virus; these 6 sera were from persons of various ages, and only 1 of 19 persons aged 80 or more showed antibody. Sera collected in 1955 and pooled according to age in 2-year age-groups, between the ages of 2 and 78, were uniformly negative for Asian-virus antibody. This was in striking contrast to the postepidemic experience: 44% of 637 sera taken last November had antibody—a remarkable tribute to the powers of spread of the virus in this country. The findings of CLARKE et al. do not support the idea that Asian antibody in pre-epidemic sera was present in any particular age-group. In addition, CLARKE et al. examined sera from 168 young people, mostly aged 18–25, who were vaccinated in 1955 and 1956 with vaccine which did not contain Asian virus. When the same sera, which had been kept stored, were subsequently tested 5% were found to have had a rise in antibody to the Asian virus. Essentially the same finding was noted by MULDER

1. Meyer, M. H., Jr., Hilleman, M. R., Miesse, M. L., Crawford, I. P., Bankhead, A. S. *Proc. Soc. exp. Biol., N.Y.* 1957, **95**, 609.
2. Mulder, J. *Lancet*, 1957, ii, 334.
3. Davenport, F. M., Hennessy, A. V., Francis, T., Jr. *J. exp. Med.* 1953, **98**, 641.
4. Laidlaw, P. P. *Lancet*, 1935, i, 1118.
5. Shope, R. E. *J. exp. Med.* 1936, **63**, 669.
6. Davenport, F. M. *Publ. Hlth Rep., Wash.* 1958, **73**, 133.

and MASUREL, who report that of 323 people of various ages vaccinated in 1956 and early 1957 9% subsequently had antibody to the Asian virus in their sera. The only obvious explanation is that the Asian virus is not so completely unrelated to previous influenza viruses as is suggested by direct cross-testing with animal sera in the hæmagglutination-inhibition test; and this conclusion is strikingly confirmed in the paper by Dr. HENLE and his colleagues (p. 818). They found that by means of a complement-fixation test which they have recently developed, and which uses the V (or viral-specific) antigen extracted from the virus, it was possible to demonstrate antigenic relationships between the Asian virus and three viruses isolated in 1933, 1951, and 1953. This cryptic relationship had not been suspected from the results of direct hæmagglutination-inhibition tests, and it may explain why antibody to Asian virus can develop in young people vaccinated with influenza viruses apparently quite different from the Asian virus.

How then are we to account for the fact that before the Asian epidemic those with Asian antibody were concentrated in the older age-groups? A hint is given in the report by Dr. HOLLAND and his colleagues (p. 820). They found that Asian virus given as a single dose of vaccine induced a very poor antibody response. By contrast, the same dose of vaccine given to people previously infected with Asian virus or to people who had previously been given one dose of Asian-virus vaccine led to a good antibody response. By extending this finding we could postulate that repeated infection of people over many years with viruses containing a cryptic "Asian" antigen could have induced Asian antibody, whereas single infections would not have done so; and it is among older people that repeated infections of this kind would be expected to occur. This hypothesis is strengthened by the finding of HENLE et al. that in guineapigs given repeated intranasal inoculations of different viruses a very specific antibody response gradually broadened to embrace more and more viruses, including the Asian virus, which had not been included among the viruses inoculated.

This reasoning is in line with that of HILLEMAN et al.,[7] who have studied the distribution of antibody to Asian virus in pre-epidemic sera among different age-groups in the population near Washington. They were concerned with one technical aspect of the hæmagglutination-inhibition test—that treating the sera with *Vibrio choleræ* filtrate may destroy traces of antibody along with normal inhibitors of agglutination. When they used a strain of virus which was not sensitive to these normal inhibitors, and thus were able to avoid using *Vibrio choleræ* filtrate, they found that the age-distribution of Asian-virus antibody was not sharply confined to older people; there were low antibody levels in people aged 20–40, and the levels rose gradually to a maximum in people aged 50–59 and remained the same thereafter. This technical factor may explain the differences in age-distribution found by different investigators. But HILLEMAN et al. also show, as did HENLE et al. by an independent technique, that the distribution of antibody to older strains is not confined to people who were alive at the time when these strains were prevalent. The same finding was noted in the sera of Nigerians by ISAACS,[8] who concluded that antibody to an influenza virus could not be taken as evidence of infection with that particular virus, but might result from infection with strains with which it shared minor antigens. Thus it seems that the antibody spectrum in the population does not sharply reflect previous experience with influenza viruses; the mirror images are blurred, and we should beware of overestimating our powers of focusing them.

There is a practical aspect of this controversy in connection with influenza vaccines. DAVENPORT,[6] who has accepted the idea that the 1957 virus is very similar to the 1889 virus, takes this conclusion as evidence for his belief that influenza viruses contain a finite number of antigens and that the viruses of the past will reappear as immunity to them in the population gradually recedes. DAVENPORT believes that if the number of antigens in the influenza virus is relatively small it will be possible to prepare a polyvalent vaccine which would protect against all the possible antigenic forms that the influenza viruses could assume. Alternatively, if influenza viruses can mutate freely there is little to be gained by this approach to influenza vaccination, and vaccines should incorporate up-to-date viruses and thus at least take account of the most recent major antigenic change of the virus. As with most theoretical arguments, theories are of little account compared with facts. The only way to settle this controversy is to compare the protective power of polyvalent vaccines made from older strains with vaccine made from a more up-to-date strain. This was in fact done in the recent epidemic. In this country the Medical Research Council's Committee on Influenza Vaccine Trials [9] found in a carefully controlled trial that a polyvalent vaccine containing three older influenza-A viruses gave no protection, whereas a monovalent vaccine containing the Asian virus gave approximately 67% protection. In a similar type of trial at Great Lakes Naval Training Centre in the U.S.A., a polyvalent vaccine without Asian virus is reported to have caused slight protection, estimated as 45%, which was less than that found with adequate doses of monovalent Asian vaccine.[10] Experience in these trials and in previous ones in 1947–48 seems to warrant the conclusion that when a major antigenic change in the influenza virus has taken place vaccines made with older strains are unlikely to give a useful degree of protection, whereas vaccines made with the epidemic virus can give reasonable (although by no means complete) protection. On the other hand, when slight antigenic changes in the virus take place there is little to be gained by using the most up-to-date virus, and the use of

7. Hilleman, M. R., Flatley, F. J., Anderson, S. A., Luecking, M. L., Levinson, D. J. *New Engl. J. Med.* (in the press).

8. Isaacs, A. *J. Hyg., Camb.* 1957, **55**, 485.
9. Medical Research Council Committee on Influenza and Other Respiratory Virus Vaccines. *Brit. Med. J.* Feb. 22, 1958, p. 415.
10. Commission on Influenza of the Armed Forces Epidemiological Board. *J. Amer. med. Ass.* 1957, **165**, 2055.

recent and related viruses should be just as effective.

As to the whereabouts of the 1918–19 virus and whether something similar to the pandemic of that time will ever recur, we are as much in the dark as before. But one thing is clear—there is less excuse than ever for relaxing our watch on the influenza viruses.

## Cancer of the Large Bowel

WITH scrupulous attention to history and examination the diagnosis of cancer in the large bowel should not often be missed. From an analysis of 1023 cases in the U.S.A., POSTLETHWAIT et al.[1] have found abdominal pain and change in bowel habit or character of the stool to be the predominant symptoms; and MUIR [2] reports similar findings in 714 patients in this country. But there is an odd discrepancy between the two series. In the American cases bleeding was the commonest symptom of rectal cancer and the second commonest of cancer elsewhere in the large bowel. In the British cases bleeding was one of the main symptoms in less than 10% of patients with neoplasms in right or left colon, in 30% (fourth in order of precedence) of those with neoplasms in the sigmoid, and in 66% (second place to "bowel complaint") when the rectum was involved. Perhaps cancer education has caused American patients to become more observant and less phlegmatic than the British.

It is an odd paradox that investigations can sometimes put us off the diagnostic scent. Many patients now present themselves with vague abdominal symptoms requiring investigation to exclude organic disease, and a negative result may wrongly be given greater weight than the evidence of symptoms or signs. RAMSAY [3] has drawn attention to this danger: in six years at the Gordon Hospital, London, 2325 barium enemas were undertaken and 151 patients with colonic cancer were treated. Of these 151, 75 had been radiographed; and a negative report had been given in 10, leading to delay in diagnosis in 7—despite sufficient clinical evidence to warrant laparotomy. A history or symptom suggesting carcinoma should take priority over a normal radiographic appearance; and radiographic evidence should be allowed to outweigh clinical evidence only when X rays show positive changes.

Recurrence at the suture-line after resection remains a problem.[4] The mechanism is uncertain; GOLIGHER et al.[5] and COLE [6] believe that implantation of malignant cells at the time of operation is an important cause. Certainly such cells do exfoliate from the lesion—a process presumably encouraged by operative manipulation. Indeed POMERANZ and GARLOCK [7] suggest that recurrences are brought about in the wound and peritoneal cavity by exfoliated cells transported there on the surgeon's gloves. GOLIGHER et al., who were concerned with sphincter-saving resections for growths of rectum or rectosigmoid, thought that possibly only half of 23 recurrences could be explained on the implantation hypothesis, others being due to fresh lesions or incomplete removal of the original one. Likewise of 108 recurrences seen at the Mayo Clinic after anterior resection, 12 were attributable to incomplete excision, and 7 to further neoplastic degeneration in a potentially malignant mucosa.[8] In the rest (less 10 cases in which the original specimen could not be examined) there was no clear explanation other than by the implantation theory; and LOFGREN et al.[8] observe that this would explain why recurrence at the suture-line is independent of lymph-gland metastasis and takes place soon after operation. The Mayo Clinic series were compared with a control group of 102 patients who survived anterior resection for five years; no significant features could be found on examination of the specimens from the two groups. COLE and SOUTHWICK [9] have found that malignant cells can be detected growing inside the veins at the tumour site or close by, and that such cells appear in a venous perfusate of the lesion; thus this type of recurrence may be caused as much by local venous invasion as by the intramural and pericolic retrograde lymphatic spread suggested by BEAL and CORNELL,[10] in whose series lymph-node involvement and invasion of the entire colonic wall was common at the primary lesion—in contrast to experience at the Mayo Clinic.[8] In addition to the technical precautions suggested by COLE to minimise the possibility of implantation (namely, isolating the growth with tape ligatures placed round the bowel) and by POMERANZ and GARLOCK (who cover the surface of the lesion), BEAL and CORNELL suggest that the limits of resection should be extended.

In 19 of BEAL and CORNELL's 21 cases of recurrence after resection in 140 patients, the original growth was on the left side. Such a preponderance of recurrence, not noted in the other series, could be explained by the fact that this is the common site for polyps, the inference then being either that recurrence is due to small polyps at the suture-line not observed at operation (in 1 post-operative death a residual papilloma was found adjacent to the anastomosis) or that polyps developing in the natural course of events cause the primary lesion and develop again in the predisposed mucosa on either side of the anastomosis. But opinions are divided as to whether small papillomas are sinister; GRINNELL [11] maintains that they are not if the lesion is less than 1 cm. in diameter, while WEINGARTEN and TURELL report malignancy in polyps as small as 3 mm.[12] FIGIEL et al.,[13] who can demonstrate small lesions of the colon with greater ease by their high-voltage "spot-compression" technique, suggest that small asymptomatic polyps beyond the range of the sigmoidoscope do not require extirpation provided the patient is kept under surveillance. This raises the important issue whether all colonic polyps—adenomatous or papillo-

1. Postlethwait, R. W., Adamson, J. E., Hart, D. *Surg. Gynec. Obstet.* 1958, **106**, 288.
2. Muir, E. G. *Brit. J. Surg.* 1956, **44**, 1.
3. Ramsay, G. S. *ibid.* 1956, **43**, 576.
4. See *Lancet*, 1954, ii, 79; *ibid.* 1956, i, 944.
5. Goligher, J. C., Dukes, C. E., Bussey, H. J. R. *Brit. J. Surg.* 1951, **39**, 199.
6. Cole, W. H. *Arch. Surg.* 1952, **65**, 264.
7. Pomeranz, A. A., Garlock, J. H. *J. Amer. med. Ass.* 1955, **158**, 1434.
8. Lofgren, E. P., Waugh, J. M., Dockerty, M. B. *Arch. Surg.* 1957, **74**, 825.
9. Cole, W. H., Southwick, H. W. *J. Amer. med. Ass.* 1954, **155**, 154.
10. Beal, J. M., Cornell, G. N. *Ann. Surg.* 1956, **143**, 1.
11. Grinnell, R. S. *Surg. Gynec. Obstet.* 1958, **106**, 288.
12. Weingarten, M., Turell, R. *J. Amer. med. Ass.* 1952, **149**, 1467.
13. Figiel, S. T., Figiel, L. S., Rush, D. K. *ibid.* 1958, **166**, 1269.

matous, large or small, on the right side or the left—should be regarded as premalignant and treated accordingly. Correlation between the incidence of polyps and that of cancer is not immediately obvious; in 50,000 routine proctosigmoidoscopic examinations PORTES and MAJARAKIS [14] found polyps in 7·9%, cancer in 0·685%. This question is important in management, for already LILLEHEI and WANGENSTEEN [15] have advocated total or subtotal colectomy for cancer distal to the hepatic flexure and similarly for right-side lesions provided no more than 20 cm. of ileum has to be removed (if more is taken, then the sigmoid may need to be retained in order to avoid diarrhœa following ileoproctostomy). Further support for this approach has come from TEICHER and ABRAHAMS [16]; but GRINNELL,[11] after studying 1335 cases with adenomas and papillomas, found that only 1 in 67 might have benefited from such major procedures; and 8 out of 66 with multiple cancers would have similarly benefited—this representing 0·73% of 1083 cancer resections during the period under review. WAKELEY and GRAVES [17] remark that simple removal of a papilloma that is proved histologically to be carcinomatous is sometimes not followed by recurrence. TURNBULL,[18] who reports on 86 patients treated for carcinoma in polyps of the colon and rectum, considers that no hard-and-fast rules can be set forth for their treatment.

## Cerebral Palsy

CEREBRAL palsy is a topic that bristles with difficulties, and one of the sharpest bristles is the nosological. The term includes a variety of lesions of the brain, each with various origins and various clinical manifestations. It has some merit in that patients with cerebral palsy (which may be defined as a congenital motor deficiency that is not progressive) tend to have certain needs in common; but it has drawbacks too, in that the needs of children with cerebral palsy, so defined, differ from case to case, and overlap those of some children with acquired lesions (e.g., from encephalitis early in life) who present a similar clinical picture. Not only does the nature and severity of the motor defect vary widely; but some children have also severe mental defect, others little or none; some have fits, some athetosis, others neither; about 20% have severe hearing defects, which may not be detected until audiometry is done [19] and may be misdiagnosed as mental defect; and some (as many as 50%) have impaired sensation, the importance of which is just being recognised—it is of little use to train a child to use a limb that he cannot feel.[20] Moreover, family circumstances (the income and intelligence of the parents, the presence of siblings, and the geographical situation of the home) partly determine the needs of individual patients. "Go in fear of the abstract" was EZRA POUND's advice to poets: "go in fear of the general" might be a good motto for doctors, especially where the particular circumstances and needs range as widely as they do in cerebral palsy.

There is no cure for cerebral palsy; the damage to the brain, or failure in its development, cannot be made good. But much can be done to help muscle development and coordination, by making the most of the power that remains, and perhaps by bringing to the surface dormant reflex patterns that are not used by people with undamaged brains.[21] Drug treatment may help: K. H. SPARUP, in a letter,[22] and ALAN MONCRIEFF, in a lecture to the British Council for the Welfare of Spastics,[20] have referred to the varying results when primidone is given for athetosis associated with cerebral palsy, and meprobamate for spasticity or athetosis. There is also a place for operation: in some cases hemispherectomy has abolished fits and temper tantrums without making the paralysis worse.[23 24] There is some hope that athetosis may be improved by a method, mentioned by Professor MONCRIEFF, of injecting alcohol, with or without celloidin, into the corpus striatum; but such techniques are still being developed and tested, and though it is of great value to remove the handicap that athetosis or epilepsy adds to the paralysis, the chief disability remains.

It is very important, then, that the child with cerebral palsy should have the best possible treatment for his motor defect; this treatment is educative, and to be effective must begin soon. The aim, at least in some centres, is to make as many as possible of these children capable of going to normal schools at school age,[25] which means that the diagnosis must be reached as early as possible—and that, once this has been done, treatment must not be delayed. At present the delay is often too long. Dr. LAWSON, in his account (p. 840) of the cerebral-palsy unit at Queen Mary's Hospital, Carshalton, says that only a tenth of the patients were referred in the first eighteen months of life, and a third were over the age of 5 years, while INGRAM [26] found that only 4 of 79 spastic children were correctly diagnosed in the first year. Early diagnosis is far from easy. MONCRIEFF mentions such slight signs as "a little undue flabbiness, a rather suspicious rolling of the head . . . there is often a suspicious sort of rigidity present"; and he refers to the spastic tone of the spastic child, contrasted with the plastic tone of the athetoid child—"there is a feeling about the movements which those who work with these children know about, which, as we have found, is difficult to explain to other people". Those in the best position to detect cerebral palsy early are child-welfare workers and the family doctors who take a special interest in babies, who are most likely to detect slight differences from the normal. Ideally all babies should be examined periodically by a doctor; and such examination is definitely necessary wherever there has been any complication of pregnancy, labour, or the neonatal

14. Portes, C., Majarakis, J. D. *ibid.* 1957, **163**, 411.
15. Lillehei, R. C., Wangensteen, O. *ibid.* 1955, **158**, 163.
16. Teicher, I., Abrahams, J. I. *Surg. Gynec. Obstet.* 1956, **103**, 136.
17. Wakeley, C., Graves, F. T. *Lancet*, Feb. 15, 1958, p. 329.
18. Turnbull, R. B. *Dis. Colon Rectum*, 1958, **1**, 44.
19. Fisch, L. *Lancet*, 1955, ii, 370.
20. Moncrieff, A. Cerebral Palsy Today: an address to the British Council for the Welfare of Spastics, 13, Suffolk Street, Haymarket, London, S.W.1. 1957. Pp. 15. 1s. 6d.
21. *Lancet*, 1954, ii, 746.
22. Sparup, K. H. *ibid.* 1957, ii, 807.
23. Krynau, R. A. *S. Afr. med. J.* 1950, **24**, 539.
24. McKissock, W. *Proc. R. Soc. Med.* 1953, **46**, 431.
25. *Lancet*, 1954, i, 90.
26. Ingram, T. T. S. *Arch. dis. Childh.* 1955, **30**, 244.

period. But making a firm diagnosis requires a good deal of experience of cerebral palsy: indeed, Dr. LAWSON holds that about 50 new cases must be seen every year if facility is to be acquired in diagnosis and treatment. The work of such a special diagnostic unit includes estimation of intelligence as well as of motor function; in the children with cerebral palsy the prognosis and treatment depend in part on the mental ability. Those with normal intelligence can often learn to use their motor system in such a way that no deformity develops.[27] It is of course far from easy to estimate intelligence in infants; but some useful tests are given by Mrs. COLLIS.[28]

When the diagnosis has been made, treatment must begin at once, to prevent abnormalities of function and structure. But in each case the physician must decide, not only the treatment given, but also who is to give it, and where. In the article we published last week Dr. ELLIS estimates the part that individuals and voluntary agencies must play, and the responsibility of society in providing the range of institutions needed. Surveying the provision made for 133 cerebral-palsy children of school age in three local-authority areas, he contrasts it with the provision he regards as desirable. He would have fewer patients attending normal schools because many had "specific learning difficulties or were so backward that they needed more individual help than their teachers could afford to give them". He thinks that a much larger proportion should attend schools for the educationally subnormal—of which there is a general shortage. About a third, he believes, should be in schools or occupation centres specially established for children with cerebral palsy. Dr. LAWSON suggests that children with cerebral palsy should go to the type of school most suitable in each individual case, but be grouped in certain schools in a wide area: this would ease cooperation between the schools and the cerebral-palsy service. Both Dr. LAWSON and Dr. ELLIS emphasise the importance of parents being instructed and taking part constantly in the treatment when the child is living at home.

Even in a closely packed community such as ours there are geographical difficulties. At Dr. LAWSON's clinic, 40% of the patients are referred from places more than 50 miles away; and in such cases little can be done besides making a diagnosis, unless patients are admitted, which is undesirable for more than a very few. The answer is not to set up such clinics everywhere, because (Dr. LAWSON estimates) a catchment area with a population of 2 million is needed to provide the 50 new cases a year that the staff must see to get enough experience. Such clinics should probably be at hospitals, because for complete diagnosis audiometry, electroencephalography, and other aids are sometimes wanted. There is a need for perhaps one or two diagnostic clinics in each great city or conurbation, but (apart from exceptional cases) they need treat only the children who live on their doorstep. Most of the rest could probably be treated adequately in the various kinds of institution specified by Dr. ELLIS, with guidance by the special diagnostic centres, which could serve both as examples of the best in treatment and as places where new methods are explored. And in our concern for children, we must not forget the needs of the increasing numbers who survive to adult life with cerebral palsy. On p. 842 Dr. PALMER reminds us of their special problems and shows what can be achieved.

Finally, Professor MONCRIEFF wonders whether a child with cerebral palsy should ever go to a normal school. Among the often neglected disabilities to which he draws attention, besides deafness and sensory defect, is the emotional warping. He quotes R. K. BYERS, of Boston, as saying that the yardstick of successful treatment now is not motor development but emotional adjustment. The child with cerebral palsy is not a source of joy to his parents, and is surrounded by anxiety. More interest than hitherto should be given to supplying emotional and sensory experience, instead of concentrating only on motor defects. The child with cerebral palsy differs much from a child of the same intellect and motor disability who lived a normal life for a few years before having, say, poliomyelitis; and the same type of school may not be suitable for both. "It is something to be worked out". A spastic child may be distracted, bewildered, and upset among normal children, and may even make better progress in isolation.

It is clear that, on many topics, those who have done most work on cerebral palsy are not in agreement. We need more exact knowledge of the results of various methods of management, and investigations into the causes and prevention of cerebral palsy; not so much now by retrospective inquiry as by prospective and physiological investigations. The therapeutic work is as important as it is valiant, and will long be needed; but there is a limit to what even the most devoted and skilful therapist can do, and we must find ways of preventing the disability more often. The two national societies have done a valuable service in calling attention to cerebral palsy, stimulating research, and coordinating activity. So far as the medical profession is concerned, this is being continued by the National Spastics Society's issue of a new quarterly journal, the *Cerebral Palsy Bulletin*,[29] edited by Dr. E. CLAYTON-JONES, which hopes to "stimulate interest in the scientific and clinical aspects of the various forms of cerebral palsy". This issue contains a brief biography of LITTLE (which recalls that his first account of "Little's disease" appeared in this journal[30]) and a reprint of his paper read to the Obstetrical Society of London in 1861, based on 200 cases he had seen. The next issue will contain abstracts from and comments on recent publications.

The two national societies may be relied on to go on with their excellent work; but we must agree with Professor MONCRIEFF that it is not in the best interests of the patients (or of those whose admirable voluntary efforts are duplicated) that there should be two societies; and we hope that means can be found for their fusion.

27. Collis, E. *Lancet*, 1953, ii, 757.
28. Collis, E. *ibid.* 1953, i, 416.
29. *Cerebral Palsy Bulletin*, 1958, no. 1. Published for the medical advisory committee of the National Spastics Society, 28, Fitzroy Square, London, W.1. Pp. 36. 2s. 6d.
30. Little, W. J. *Lancet*, 1843-44, i, 318, 350.

# Annotations

## USE AND TOXICITY OF SULPHONAMIDES

SULPHONAMIDES have been in use for over twenty years. Starting with the original 'Prontosil Rubrum', the aim has been to find derivatives which are more potent in antibacterial activity and less toxic to man. It is an advantage if the frequency of administration can be reduced, so that disturbance of the patient at night can be avoided without the blood-level falling below that required for therapeutic effect. The sulphonamides now in common use, either singly or in various mixtures, for the treatment of systemic infections include sulphathiazole, sulphadiazine, sulphamerazine, and sulphadimidine.

It is doubtful whether, as regards antibacterial activity, there is much difference between these four compounds. The choice should accordingly be based on toxicity, absorption, persistence of effective concentration in the blood, and frequency and convenience of administration. In these respects the four differ considerably. Sulphathiazole is undoubtedly the most toxic, being especially liable to cause rashes and drug fever. It and its acetyl derivative are relatively insoluble in acid urine; it is rapidly excreted, and frequent administration is required to maintain an adequate blood concentration. Sulphathiazole appears in the *British National Formulary, 1957* but is omitted from the *British Pharmacopœia, 1958*. Sulphadiazine and sulphamerazine are less liable to cause generalised toxic effects; but they and their acetyl derivatives are relatively insoluble in urine. Dr. Arneil, in his article this week, draws attention again to the particular danger of sulphamerazine causing hæmaturia in children. Sulphadimidine is safer since it is relatively soluble, even in an acid urine, in both its free and acetylated form.[1]

The risk of injuring the kidneys with sulphathiazole, sulphadiazine, and sulphamerazine may be reduced by ensuring a high fluid intake to increase the volume of urine and by making the urine alkaline. Unfortunately, these precautions are troublesome and sometimes neglected, and often insufficient alkali is given. Recognising these difficulties, Lehr [2] introduced the principle of sulphonamide mixtures to reduce the liability to crystal formation in the urine. The tendency to crystal deposition varies with the concentration of each individual sulphonamide, and thus is considerably less in a mixture of several compounds; but the therapeutic effect is that of the total concentration. The *National Formulary* describes trisulphonamide tablets for adults and a mixture for infants containing sulphathiazole, sulphadiazine, and sulphamerazine.

The question arises whether there is still any place for these more toxic sulphonamides, even in mixtures; for many antibiotics, on the whole less dangerous than the sulphonamides, have been introduced—including phenoxymethylpenicillin, which can be given by mouth. There is probably no sufficient reason for retaining the relatively toxic sulphathiazole in sulphonamide mixtures.[2] The closely related compounds—sulphadiazine, sulphamerazine, and sulphadimidine—differ little from sulphathiazole in their absorption, their penetration into the cerebrospinal fluid, and the ease with which a therapeutic blood-level is maintained. Sulphadimidine shows slightly greater plasma binding and conjugation than the other two compounds,[3] but it is doubtful whether this substantially affects therapeutic efficacy. Sulphadimidine is much less likely to cause renal damage, and is therefore preferable certainly to any single component of the official mixtures and probably to the mixtures themselves. The practising doctor may be well advised to avoid entirely the more hazardous preparations—sulphathiazole, sulphadiazine, and sulphamerazine—either singly or in combination with each other or with antibiotics. This applies especially to sulphamerazine for children, in whom the risk of hæmaturia is particularly great. If administration of sulphadimidine is not followed by adequate response, a change should be made to a suitable antibiotic and not to another sulphonamide or a mixture of sulphonamides. On the other hand sulphadimidine (and possibly newer equally non-toxic sulphonamides which have not been so fully evaluated) still have a definite place in therapeutics. They are especially valuable in meningococcal septicæmia and meningitis, and in certain urinary-tract infections. But the use of even these sulphonamides is not without risk, and attention must always be paid to dosage, renal function, and fluid intake.

1. Goodman, L. S., Gilman, A. The Pharmacological Basis of Therapeutics; p. 1296. New York, 1955.
2. Lehr, D. *Brit. med. J.* 1947, ii, 943.

## THIRST

THIRST—the uneasy or painful sensation caused by want of drink, as the Oxford Dictionary defines it—being subjective is difficult to investigate. But if it can be assumed that in laboratory animals drinking implies a state analogous to thirst, then a dry mouth is not the whole story [4] and a "drinking-centre" exists. Pure water-deficiency results in thirst; but hyperosmolarity is unlikely to play a large part because the hyperosmolarity associated with other disturbances—for example, increased blood-urea—does not increase thirst unless there is an accompanying diuresis. A change in the distribution of body-fluid may be important. Thus, salt depletion can give rise to a sensation of thirst that is not slaked by pure water but can be relieved by small amounts of hypertonic saline solution.[5] Salt depletion causes the extracelilular-fluid volume to contract, and it seems that shrinkage of this volume results in the urge to drink. Removal of a large volume of extracellular fluid, such as isotonic ascitic fluid, also leads to thirst: the paracentesis cannot affect the osmotic pressure of the body-fluid, but it does affect its total volume and compartmental distribution. Thirst has been noted [6] as a symptom of impending diarrhœa, because, it is believed, of the reduction of volume of extracellular fluid following sequestration of isotonic fluid in the lumen of the intestine. It seems, therefore, that although a rise in the osmotic pressure of the body-fluids without change in volume *may* lead to thirst, changes of the volumes in fluid compartments *always* lead to thirst.

Most of the work on the neural integration of thirst has been done in goats. Polydipsia results from hypothalamic stimulation, either by local injection of 2% sodium chloride or by electrical stimulation.[7] Direct evidence of a "drinking-centre" in man is difficult to obtain, though rare cases are described in which diabetes insipidus and anterior-pituitary insufficiency together allow a greater loss than intake of fluid, leading to hyperosmo-

3. Lehr, D. *ibid.* 1950, ii, 601.
4. Cannon, W. B. *Proc. roy. Soc.* 1918, **90**, 283.
5. McCance, R. A. *Lancet*, 1936, i, 823.
6. Strauss, M. B. *Arch. intern. Med.* 1958, **101**, 216.
7. Andersson, B., McCann, S. M. *Acta physiol. scand.* 1955, **33**, 333.

larity of body-fluids. The effect of impulses from peripheral nerves is evident in the influence on the drinking response of a dry mouth and of gastric distension with a balloon,[8] and in the pharyngeal "metering" of fluid intake in dogs with œsophageal fistula.[9] The evidence so far has led to the postulate [10] that the hypothalamus contains receptors which regulate water intake as well as output; and presumably receptors concerned with intake are stimulated, partly by changes in the volume of the fluid compartments, and partly by afferent impulses from the gastrointestinal tract.

## CERVICOTHORACIC GANGLIONECTOMY

THE results of cervicothoracic ganglionectomy in the treatment of arterial lesions reflect the selection of patients submitted to operation rather than the particular technique of sympathetic interruption. Raynaud's disease as defined by Allen and Brown [11] must have been present bilaterally for at least two years; the colour changes occur on exposure to emotion or cold; and gangrene or any primary associated disease such as acrosclerosis are absent. Gifford et al.[12] review 70 such patients, all women and mostly below 40 years of age, who some years ago were submitted to resection of the stellate ganglion, and often the second thoracic. Their results mirror those already published: less than half the patients definitely benefited, and in some the disability was actually enhanced. Gifford et al. agree that the results in secondary Raynaud's phenomenon, such as may accompany acrosclerosis, are the worst, while those in the lower limb are better than those in the upper limb. Their data do not reveal any way by which the results of sympathectomy in the upper extremities can be predicted in advance, except that good results were obtained more often when complications of Raynaud's disease, such as nutritional changes, were not present before operation. Before deciding to operate it is important to exclude the many other conditions which may be associated with digital colour changes—particularly the so-called collagen diseases. Most patients with these other disorders are in no way helped by sympathectomy, and in some the primary disease may be aggravated. Raynaud's phenomenon due to a local fault, such as sometimes follows prolonged use of a vibratory tool, is not benefited; but where the sympathetic impulses play an essential part in the causation of symptoms interruption of the nervous control will be followed by great relief. What is much needed now is a simple clinical test to establish the relative importance of the various factors which contribute to the Raynaud phenomenon.

## IMMUNOLOGY

IN view of the importance of immunological phenomena in medical and veterinary practice as well as in the wider fields of biology, it is surprising that hitherto Britain has had no scientific society devoted mainly to advancing our knowledge of immunity. In many countries—notably the U.S.A. and Germany—active immunological societies with specialised journals of international repute have existed for many years. In recent years the scope of immunology has increased enormously; and it now encompasses the increasingly important subjects of allergy, auto-antibodies and their possible role in the pathogenesis of many common diseases, and homograft immunity and acquired tolerance. In addition, it has a large stake in genetics, mainly by virtue of its importance in the realm of blood-groups and blood-group substances, as well as lesser but none the less important interests in the pathogenesis of tumours. On a slightly less biological level it claims many devotees in the fields of pure chemistry and physics. This growth pressure led to the formation, in the autumn of 1956, of the British Society for Immunology. The necessity for a journal of its own was immediately appreciated by the new society; and within fourteen months of the inaugural meeting there has appeared the first issue of *Immunology*,[1] the society's official journal, under the editorship of Prof. J. R. Marrack.

This issue confirms the greatly widened range of the subject. Thus the opening paper, by P. B. Medawar and P. S. Russell, on adrenal homografts in mice with special reference to immunological adrenalectomy, deals with how to overcome the immune reaction that at present vitiates the most skilful attempts to transplant tissues from one individual to another. The paper by B. Cruickshank and A. R. Currie on the localisation of tissue antigens by the fluorescent antibody technique is a further example of the extension of this exciting immunological method [2] into other fields of physiology and pathology. Other contributors show well the present physical trend in immunology; and the more chemical approach is represented by a study of the components of mycobacteria that influence antibody production.

## A CHAIR OF PÆDIATRIC SURGERY

THE news of the appointment of Mr. A. W. Wilkinson as the first professor of pædiatric surgery at the Institute of Child Health in the University of London (see p. 861) is of exceptional interest; for there is only one similar chair in the world—at Boston, Massachusetts. It is fitting that such a chair should be established at the Institute; for the associated Hospital for Sick Children, Great Ormond Street, has been the scene of pioneer work on surgery in the young, which the new academic unit will be able to consolidate. This development has been made possible by a gift of £80,000 from the Nuffield Foundation, to mark Lord Nuffield's 80th birthday. It was at the Institute that in 1945 the first Nuffield chair—that of child health—was created.

## THE BUDGET

IN the past year the level of unemployment has risen from 1·7% to 2·0%. Mr. Heathcoat Amory, the Chancellor of the Exchequer, when he introduced his first Budget last Tuesday, would no doubt have liked to stimulate demand by sweeping cuts in taxation. But Britain's falling share of world trade, and the continuing need to strengthen sterling, prevented such a move; and his main tax concession consists in curtailing the rate of purchase-tax on goods subject to this tax at the highest rates. The limits of income-tax exemption for the elderly are to be slightly raised, and the aged relief limit is to go up from £700 to £800. These concessions, though they are not large and affect only some of the elderly, give welcome recognition to the difficulties of this section of the population in making ends meet.

8. Montgomery, A. V., Holmes, J. H. *Amer. J. Physiol.* 1951, **167**, 811.
9. Bellows, R. T. *ibid.* 1939, **125**, 87.
10. Andersson, B., McCann, S. M. *Acta physiol. scand.* 1955, **35**, 191.
11. Allen, E. V., Brown, G. E. *Amer. J. med. Sci.*, 1932, **183**, 187.
12. Gifford, R. W., Jr., Hines, E. A., Craig, W. McK. *Circulation* 1958, **17**, 5.

1. *Immunology*. Published quarterly by Blackwell Scientific Publications, Oxford. £3 per annum. Manuscripts should be addressed to the editor at the Department of Pathology, University of Cambridge.
2. See Glynn, L. E., Holborow, E. J., Johnson, G. D. *Lancet*, 1957, ii, 1083.

## Special Articles

# A CEREBRAL-PALSY SERVICE FOR CHILDREN

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THE cerebral-palsy unit at Queen Mary's Hospital for Children, Carshalton, has been running continuously since 1943, and the parental-advice clinic since 1945. In August, 1957, 157 patients were in the care of this service. 17 were in the residential unit and 140 were attending the advice clinics with their parents. Of these 140, 59 had attended for up to three years, 47 for from three to six years, 27 for from six to nine years, 6 for from nine to twelve years, and 1 for thirteen years.

This article analyses the experience of the diagnostic clinic and of the new entrants to the advice-clinic service over the years 1954–56, during which time 206 cases were referred.

The principles underlying the running of this unit have been described by Collis et al. (1956), and only the structure of the service will be outlined here.

There is an inpatient unit of 20 beds, within a general children's hospital, working in close cooperation with a hospital school, and including on its staff two specially trained teachers.

New patients are seen with their parents at a diagnostic clinic where, following history-taking and examination, a decision is taken on the following questions:

1. Is this a case of cerebral palsy?
2. If it is, what type is it, and to what extent, if at all, is there evidence of a complicating mental defect?
3. Are there already incipient or established secondary deformities?

In difficult cases a decision may be delayed until after a period of observation in the inpatient unit.

The prognosis, both physical and mental, is then explained to and discussed with the parents, and the services of the advice clinic are offered to them.

They are told that the day-to-day management and guidance of their children does not need any special technical facility, and that affected children will make better and faster progress if they are looked after by their parents. The day-to-day continuity of treatment needed is such that nobody but the parent can carry it out, unless the child is to be admitted for a very long period to a heavily staffed unit, and thus separated from his home for long periods during his formative years. When parents accept this offer, advice-clinic visits are arranged at about monthly, and later at longer, intervals.

The limited purpose of what follows is to analyse the initial assessment of cases and the extent to which advice-clinic services are accepted and used, and to point to certain unresolved problems which may be of wider interest.

### ANALYSIS OF CASES

Of the 206 patients referred to the clinic in 1954–56, 68 were found to have mental defect only, and the parents were given advice by the almoner or referred to the mental health authorities where appropriate. 11 children were found to have neither cerebral palsy nor mental deficiency. Most of these were normal children whose progress, though it had given cause for alarm, was considered to be within the normal range. The remaining 127 had cerebral palsy in one of its forms, with or without some mental defect. These cases fell into the following clinical categories:

| | |
|---|---|
| Generalised spasticity | 76 cases |
| Variable rigidity | 19 cases |
| Athetoid cerebral palsy | 3 cases |
| Ataxia | 3 cases |
| Congenital hemiplegia | 21 cases |
| Acquired hemiplegia | 5 cases |

Of these 127, 38 did not initially accept the services of the advice clinic for various reasons, among which geographical reasons predominated. The remaining 89 accepted the service offered, but of these 28 had ceased to attend within a few months. The reasons for this cessation were again largely geographical; but some who stopped had accepted other advice, and in some the cerebral palsy was complicated by such severe mental deficiency that institutional management elsewhere was arranged at parental request. Of the original 127 cases, therefore, only 61 (48%) effectively accepted the advice-clinic services.

This clinic acts to some extent as a reference clinic for cases over a wide area, and for those who come a long distance it is often impossible to offer more than diagnosis and initial advice. Of the 127 cases, about 40% came from the London or Surrey areas, 20% from other counties near London, and 40% from more than 50 miles away.

The services of the advice clinic are invariably offered to all who wish to come, whatever the degree of mental defect, but it is the parents of the most severely mentally affected children who most commonly fail to make consistent use of the service, because it is to them that it has least to offer.

*Intelligence*

Following clinical assessment, the cases are grouped into one of four intelligence levels, in terms of the probably appropriate form of education or training at school age:

| | |
|---|---|
| 1. Probably capable of receiving education at a normal school | 31 (24%) |
| 2. Requiring education in an educationally sub-normal school | 30 (24%) |
| 3. Borderline of educability | 18 (14%) |
| 4. Ineducable | 48 (38%) |

The probable social prognoses, taking account of both mental and physical disability, were as follows:

| | |
|---|---|
| Independent | 36 (28%) |
| Partially dependent (that is to say, probably capable in due course of taking up limited and carefully arranged employment, but not capable of living a fully independent life) | 26 (20%) |
| Dependent | 65 (51%) |

*Ætiology*

It is seldom possible to assign a cause with certainty in individual cases. For example, though there is a definite association between cerebral palsy and fœtal or neonatal anoxia, the extent of this anoxia is not measurable, and many infants suffer anoxia without developing cerebral palsy. The analysis of a large series, however, may well show significant associations. Among the various factors analysed in the case-histories, the following were found:

| | |
|---|---|
| Definite clinical evidence of neonatal anoxia | 40 cases (31%) |
| Maternal toxæmia | 10 cases (8%) |
| Long or difficult labour | 17 cases (13%) |
| Long-continued neonatal jaundice, including hæmolytic disease of the newborn | 16 cases (13%) |

Many cases of cerebral palsy could be diagnosed earlier than at present if all babies with a history of any maternal

disease or complication of pregnancy, labour, or the neonatal period were followed up carefully for a year or two. Even if this were done, however, a substantial proportion of cases would still be found to arise in babies without such histories. Of the 121 cases of congenital cerebral palsy in our series, in 43 (36%) there was no history of any of the following: antepartum hæmorrhage, anoxia, forceps delivery, maternal toxæmia, precipitate labour, long or difficult labour, long-continued neonatal jaundice, hæmolytic disease of the newborn, birth-weight under 3 pounds. It is difficult to see how these cases could be picked up at the earliest opportunity, except by a careful follow-up of all babies. In view of the very large numbers of babies concerned this could probably be done on a national scale only by the reference from baby clinics of all babies showing evidence of delay or abnormality of motor development. (In the case of the 68 children found to have mental defect only, 37 (55%) had no such history of abnormality.)

*Birthweight*

Of the 109 cases in which reliable birthweights were obtained, 6 were over 9 lb., 53 between $5^1/_2$ and 9 lb., and 50 under $5^1/_2$ lb. The incidence of prematurity was therefore 45%.

*Age at Referral*

One of the most serious practical problems arises from the late age at which children are referred to the diagnostic clinic. It is extremely important that the diagnosis should be made early, so that the baby may be appropriately handled and guided in the acquisition of motor patterns, thus making the best use of his limited capacity from the start, and avoiding so far as possible secondary disorders of function and structure. Of the 127 children, only 13 (10%) were referred in the first eighteen months of life; a further 41 (32%) between the ages of 18 months and 3 years; 29 (23%) between the ages of 3 and 4 years; and 44 (34%) over the age of 5 years.

*Mental Defect With and Without Cerebral Palsy*

To satisfy the parents of a mentally defective child that the child's life is not further complicated by a motor deficiency is a substantial and valuable part of the clinic's work. This opinion we have been able to give in 68 of the 206 cases referred to us. The cases of mental defect or cerebral palsy or both constitute between them 195 of the total number of 206 cases referred to us. These 195 cases have been classified to show the number of cases from each source and the proportion of these which were found to have mental defect only.

| *Source* | *No. referred* | *Proportion found to have mental defect only* |
|---|---|---|
| Hospital service | 76 | 24% |
| Local-authority medical officer | 25 | 36% |
| General practitioner | 42 | 40% |
| Parents | 38 | 45% |
| Lay society | 13 | 46% |

## ADMISSION TO RESIDENTIAL UNIT

Of the 86 patients who initially entered the service, 22 were admitted to the unit either for extended diagnosis or to get management firmly started along the right lines both for the mother and child, and a further 18 were subsequently admitted either because the child had difficulties in getting management effectively started as an outpatient, or to help the mother over a socially difficult period. Of these 86 cases, therefore, a total of 40 (just over 45%) spent some time in the residential unit itself. This was not a substitute for the system of parental care and guidance, but a necessary entrée to it.

## DISCUSSION

*Prompt Diagnosis*

This can probably best be secured by the reference to experienced diagnostic clinics of all infants in whom there is any suspicion of abnormality or delay in motor development.

*Early Management*

Early diagnosis is not always followed by immediate measures of management. Commonly when cerebral palsy has been correctly diagnosed in the 1st year of life the parents are told that nothing can be done until the child is 3 or 5 years of age. By this time, failure to provide day-by-day guidance of the child's developing physical activity has resulted in avoidable abnormalities of function and of structure.

*Geographical Factors*

Although this clinic operates in a fairly dense urban community, in close proximity to nearly 10 million people, 40% of the cases are referred from over 50 miles away, from which distance it is almost impossible to maintain the close contact which is needed if anything beyond diagnosis is to be offered. Nevertheless it is difficult to see how the staff of a cerebral-palsy unit can acquire facility in the diagnosis and management of these cases without a diagnostic turnover of about 50 cases a year. This turnover would correspond to the exclusive intake from a population of about 2 million (Collis et al. 1956).

*Education*

Experience shows that if the child is appropriately handled from the earliest years, so that by the time school age is reached he has at least three years of effective management behind him, he will be able to fit into the pattern of normal and special educational services provided or envisaged under the 1944 Education Act, and that the type of provision required will be decided more by his intellectual capacity than by his residual physical disability.

It is vital that there should be close cooperation between doctor, teacher, and parent, but this we find difficult to achieve if the parent has not several years of guided experience behind her before school starts, and if the children attending an advice clinic are scattered among many schools. The latter difficulty has led to the suggestion that special schools for cerebral-palsied children as such should be provided. This view overlooks the very wide scatter of intelligence level in these children, which varies between the highest and lowest intelligences for which the education authority is responsible, but with a strong bias towards the lower levels. A school for all cerebral-palsied children in the locality would, therefore, despite its small size, have to cater for a wider variation in intelligence levels than is provided for either in normal or in educationally subnormal schools.

A compromise solution might be possible at least in densely populated areas. The cerebral-palsied children could be educated in the type of school (normal, educationally subnormal, or physically handicapped) which would best suit them; but over a wide area they could be concentrated so far as possible in selected schools of the appropriate type, working in close conjunction with a cerebral-palsy advice service. Even under these conditions great care would have to be taken that each child's education was planned according to his individual requirements rather than his verbal diagnosis. This applies especially to

the more gifted children, who, because of their higher intelligence and greater learning ability, will overcome their physical disability more rapidly and more completely than others and may well be able to do without any special educational provision.

SUMMARY

In 1954–56, 206 cases were referred to the cerebral-palsy diagnostic and advisory service.

34% of these patients were found to have mental defect only. The exclusion of cerebral palsy in mentally defective children has become almost as important a part of the diagnostic-clinic service as the diagnosis of cerebral palsy itself.

Of the children with cerebral palsy, about a quarter were regarded as sufficiently intelligent to receive normal education, while nearly 40% were probably ineducable.

It is estimated that nearly a third should eventually be capable of leading a completely independent life in society, while just over half will always be fully dependent.

40% of cases were referred from distances of over 50 miles. The services of the advice clinics were offered in all cases of cerebral palsy, and were accepted in just over half the cases.

Only 10% were referred in the first 18 months of life, and 34% were already of school age at referral.

The figures confirm the ætiological importance of certain disorders or complications of pregnancy, labour, and the neonatal period in the ætiology of cerebral palsy, but in 36% of cases no such history was obtained. In 45% of cases birth was premature (under $5^1/_2$ lb. birthweight).

While accepting sole responsibility for the views expressed here, I wish to record a deep debt of gratitude to Mrs. Eirene Collis, who has been continuously in day-to-day charge of the cerebral-palsy unit since she started it in 1943, and on the basis of whose devoted work my experience of cerebral palsy has been gained in a close cooperation over the past four years.

REFERENCE

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# PRESTED HALL

## A RESIDENTIAL CENTRE FOR ADULT SPASTICS

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Prested Hall is a residential centre for thirty men and women severely handicapped by infantile cerebral palsy. It was opened by the National Spastics Society in January, 1955, and is leased to the society for a token rent. The treatment unit was built by the society in the spacious grounds attached to the Hall. This is, I believe, the only centre in the world catering for adult spastics offering residential physiotherapy, occupational therapy, and speech therapy, with an opportunity to lead a fuller life than is normally possible for a handicapped person in a home or institution.

### PROBLEM

Almost all the residents at Prested Hall are adults who have had no specific treatment for their condition and little or no special education. In 3 years, ten were admitted mainly because their parents, owing to age and infirmity, were unable to care for them. One came from a mental hospital where he had spent 30 years. Twenty-five were admitted specifically for physical treatment and training. The remaining eight were admitted from geriatric and chronic-sick units, where their companions were often more than twice their age. With improvements in the care of young spastics, and more understanding of their problems and their possibilities, the proportion of admissions in the third group should decrease. At present many of the admissions to any adult centre must be patients who have had no previous purposeful care and have been for years virtually relegated to the scrap-heap.

The spastic presents an inextricable mixture of social, emotional, and physical difficulties. Most of those who have been cared for at home have been grossly over-protected and have never been encouraged to do even simple things for themselves. Some have been dressed and undressed daily by their mothers up to the age of 30 or 40. One was kept indoors for the greater part of her life, though quite capable of using a self-propelled wheel chair. Such patients have learnt to depend on others and do not take easily to attempts to make them work towards their own improvement. Some are frustrated because their disability restricts them; some have been robbed even of the wish to do things and are beyond frustration.

For most, the first months at Prested Hall are their first attempt at living on equal terms with other people. The new adjustment is not easy. Initial reactions run the whole gamut from morbid shyness to aggressiveness. In the first months after the centre was opened, this led to very considerable difficulties, but as time has passed a nucleus has developed of well-adjusted residents whose stability is a material aid to newcomers.

On the physical side, difficulty in locomotion is probably the biggest problem. The previously untreated patient has had to make some use of his arms and hands, but has not usually been encouraged to move about. He is afraid of falling and is often handicapped by defective kinæsthetic sense in his legs and sense of balance. A good deal of incentive and encouragement is needed to make him feel that the effort and concentration demanded by learning to walk is really worth while.

### DOCUMENTATION

Records are kept of all residents. They include a family history where available; but, as one might expect with adults the history of confinement and early childhood was often unobtainable. Capability charts are kept of daily living activities. These are as simple as possible: complicated graphs have been found impracticable and unnecessary. Still photographs are taken of every resident in standard positions and are repeated yearly or after a major change in ability. Ciné photographs are also taken of each resident performing standard tasks, including eating, drinking, and moving by whatever means possible. The object is to record maximum capability, to study movement pattern, and to teach and encourage the patient. The classification of the cases seems more difficult as more experience is obtained. It appears possible to divide them only into predominantly spastic, athetoid, or ataxic types. In almost all cases they are mixed. Even in apparent hemiplegia, some defects are usually found on the opposite side. There is also a proportion of additional abnormalities, including four cases of congenital deformity of the hip, one of spina bifida occulta, one of epilepsy, five of partial deafness, two with marked nystagmus, and four with marked short sight.

CAPABILITY CHART: ASSESSMENT IN A CASE OF DOUBLE SPASTIC HEMIPLEGIA

| | | | |
|---|---|---|---|
| 1. Dressing | 3 | 16. Sitting in bath | 4 |
| 2. Undressing | 3 | 17. Washing in bath | 4 |
| 3. Buttons | 3 | 18. Brushing hair | 4 |
| 4. Shoes or boots | 4 | 19. Combing hair | 4 |
| 5. Laces | 3 | 20. Continence | 5 |
| 6. Tying a bow | 3 | 21. Sit on W.C. seat | 4 |
| 7. Callipers on and off | 5 | 22. Use paper | 4 |
| 8. Washing | 4 | 23. Flush | 5 |
| 9. Clean and cut fingernails | 4 | 24. Blow nose | 4 |
| 10. Clean and cut toenails | 3 | 25. Drink from cup | 0 |
| 11. Cleaning teeth | 4 | 26. Drink from mug | 4 |
| 12. Gargle | 0 | 27. Drink with straw | 5 |
| 13. Shaving/hair-slide | 3 | 28. Use a spoon | 3 |
| 14. Getting in bath | 2 | 29. Use spoon and fork | 0 |
| 15. Getting out of bath | 2 | 30. Use knife and fork | 0 |
| *carried forward* | 46 | *carried forward* | 96 |

| | | | |
|---|---|---|---|
| *brought forward* | 96 | *brought forward* | 141 |
| 31. Sit on normal chair | 4 | 46. Position sense | 4 |
| 32. Walk alone 100 yards | 0 | 47. Shape and texture | 3 |
| 33. With callipers | 5 | 48. Make a bed | 3 |
| 34. With sticks | 3 | 49. Replace sheets | 2 |
| 35. With crutches | 5 | 50. Turn mattress | 1 |
| 36. Walking machine | 5 | 51. Thread needle | 3 |
| 37. Assisted by one person | 5 | 52. Use needle | 3 |
| 38. Crawling 5 yards | 5 | 53. Clean shoes | 3 |
| 39. Up and down stairs | 3 | 54. Wash shirt or blouse | 3 |
| 40. Self-propelled chair | 5 | 55. Wringing | 3 |
| 41. Tricycle | 1 | 56. Pressing | 3 |
| 42. Talk | 4 | 57. Make a cup of tea | 3 |
| 43. Read | 0 | 58. Cut bread and butter | 0 |
| 44. Write with pencil | 0 | 59. Cook egg and bacon | 0 |
| 45. Type | 0 | 60. Prepare lunch | 0 |
| *carried forward* | 141 | *Total* | 175 (58%) |

Code 5, normal 4, reasonably well 3, well but very slow 2, not well, needs assistance 1, attempted 0, unable Maximum 300.

## METHOD

The centre is run with very few rules, and provides conditions as near to home as is possible with a community of this type. It has the advantage that the residents realise that there are other people with similar disabilities which they are striving to overcome. They improve with competition and an incentive is provided which they do not have at home.

The accommodation is divided into two-bedded and four-bedded rooms. Those with the most severe handicaps, dependent on wheel chairs, live on the ground floor. Washing and toilet facilities have been arranged for handicapped persons and include a wooden wheel chair for use with the shower. The cost is £12 a week for each resident. Most of this is met by the appropriate welfare authority. The National Assistance Board now contributes 40*s*. a week and 10*s*. a week pocket-money.

## TREATMENT

Treatment in the *physiotherapy* department aims at increasing the resident's ability to perform everyday activities, including dressing and washing, progressing where possible to complete independence. The methods followed at first were compiled from the normal sequences of development on the lines on which most children are treated. This did not work well with adults, who have well-established movements, usually in a bad pattern. The method now used is to facilitate the righting and protective reflexes and balancing reactions, and to treat contractures and scoliosis. One handicap common to almost all adult spastics is the malformation of their feet. This may be lessened by well-fitting surgical boots and shoes.

The aim of treatment in the *occupational-therapy* department is to develop any latent skills, to assess ability to work through various tasks and crafts, and, as in the physiotherapy department, to create as great a degree of independence as possible. The patient must be treated as a whole. It is not only the ability to do a particular task but a willingness to do it and sufficient concentration to work for an economic period. Residents are encouraged to take part in group activities such as debating, play-reading, and puppetry. A kitchen unit, provided by a local Women's Institute helps to fulfil a desire to partake in normal household activities, which have often been denied at home. It has proved one of the most successful ways of preparing residents for future independence. It was thought that many aids and appliances would be needed in the kitchen to suit the residents' disabilities. This proved to be wrong. A work-bench, oven, and sink were provided at a height suitable for a wheel chair. A pull-out table, containing holes for mixing-basins, and two hand-grips were all the aids needed. The residents solved their own problems and it was found better to encourage them to overcome their disabilities without gadgets. There was a great need for elementary education, and lessons were started in the occupational therapy department. These lessons are now being continued as a night class through the local education authorities, aided by one of the residents who has passed three subjects of his general certificate of education.

The principles which have been followed for *speech therapy* have been based on the following: general relaxation and positioning of the patient; exercises to improve control and depth of breathing; lip exercises to improve lip muscles; manipulation of the tongue, lips, and jaw to increase range of movement; stimulation of palatal movement; and mirror training to coordinate sound and movement by imitation, and to gain control of facial expression.

Eighteen patients out of thirty receive speech therapy. Only four of these can turn up the tip of the tongue on protrusion; thus sounds usually produced with the tip of the tongue on the alveolar ridge (e.g., t, d, l, n) are imperfectly formed. Inability to move the tongue to the side, occasionally only one side, is another difficulty. The tongue is often undeveloped, and moving the middle of the tongue backwards, as in eating, is defective. Eating and drinking movements are therefore taught in the same department. In one case a dental gag has been made by a local dental surgeon for a resident who is unable to close his lips. This gag contains a 'Polythene' tube and enables him to close his mouth and suck fluids. Before he can close his mouth round this he has to stimulate his lips by stroking them. It is hoped to reduce gradually the size of the gag and finally discard it. Dribbling is fairly common. It has been improved in several cases by encouraging the patient to exercise more conscious control of the swallowing reflex.

An imperfect speech pattern may be the easiest for the spastic to acquire, but where it has failed to convey the patient's thoughts it has caused frustration. In many cases correct guidance during childhood would have produced far better speech and may well have led to better understanding.

*Surgery.*—Only one resident has been operated on—for flexion contractures affecting his knees.

He was 31, and before operation walked on his toes with his knees bent to about 135° (see figure, a). These knees could not be straightened under anæsthetic. After operation his knees were straight and he could place both feet flat on the ground (b). It took 8 months of daily treatment before

(*a*) (*b*)

**Operation for flexion contracture of knees (*a*) before; (*b*) after.**

he could walk as well as before the operation. This was nearly 2 years ago, and he is now more stable than before and walking better. The delay, which might well have led to failure, was probably caused by a number of factors. The patient's pattern of walking was well established. With his feet flat on the floor there was a major change in this pattern which was very difficult for him to appreciate. This operation included a tendon release, which deprived him of part of his muscle and tendon sense, changing his reflex pattern. His drive and endurance was overestimated.

No doubt there is a place for surgery in the adult spastic, but the advantages must be very carefully considered beforehand, and endless time and patience may be needed in the after-treatment.

### RECREATION

Before their arrival the residents had had almost no experience of playing games. Their reaction to ball games was that they could not and did not want to play. This attitude changed very quickly and they now enjoy modified games of tug-of-war, cricket, croquet, and football, and take part in obstacle races. The team spirit is encouraged and teams are so picked as to balance their handicaps as evenly as possible. As a result of this, big movements, involving hand and eye coordination and balance, have improved noticeably.

The residents are encouraged to manage their own affairs through their own social committee. Entertainment for those who wish to take part is provided in the lounge in the evening, and there are frequent social outings to the theatre and places of interest.

### CONCLUSIONS

The treatment and management of adult spastics was approached with caution, and no dramatic results were expected. In the course of 3 years' experience the results have been encouraging. Only two out of eleven women residents could walk when they first came to Prested Hall. At the end of the first 8 months nine could walk on their own or with some mechanical aid. Of the men nine out of eighteen could walk, with or without aids; and this number was increased to eleven in the same period.

Given a chance to follow an occupation and to learn a remunerative trade, most residents have shown an ability to improve their dexterity. Two have achieved independence in a sheltered workshop. Four have improved enough to pass on to another of the society's centres for more advanced training. Five were discharged as unlikely to improve with further treatment. Two left because their local authorities withdrew their grants. One died as a result of an epileptic fit.

In seeking employment, one of the most difficult obstacles is the average employer's reluctance to take on a spastic—not necessarily because of his physical limitations, but because of his appearance. This should improve as the condition is more widely understood by the lay public. Another difficulty is the trade-union rate for the job. Most spastics are unable to work economically because they are slow, but they are quite capable of doing a good job, if they can be paid what they are worth and if they do not hold up a production team. The spastic's appearance suggests that he is accident-prone, but though there are two electric lathes, an electric drill, many sharp tools in the occupational-therapy department, and the usual kitchen ware in the kitchen, there have been no accidents so far. This suggests that spastics are not as clumsy as they often appear.

### FUTURE

There is undoubtedly a need for assessment and early training of spastics before admission to industry or a specific training-centre. Unfortunately there will always be those who cannot live independently or even work economically in sheltered conditions. It will be possible to make these less dependent and more able to appreciate a fuller life by a stay at such a centre, even if they eventually have to return to their homes or some type of institution. For the future we must look to the children, and if possible prevent or reduce the incidence of spastic disease; for there is no cure. With a better understanding and better treatment of spastic children, we should see less deformity, both mental and physical. When a child is found to be spastic, the aim must be maximum capability, making the most of the remaining undamaged part of the brain.

I am grateful to Dr. J. D. Kershaw, a member of the centre's committee, for his advice on this paper; to Mr. J. H. Watson, the warden; and to members of the staff whose cooperation and teamwork have made this treatment centre possible.

## AN ORAL CONTRACEPTIVE

ON April 9, at the London School of Hygiene and Tropical Medicine, Dr. GREGORY PINCUS gave the second Oliver Bird lecture, on Fertility Control with Oral Medication. Sir Russell Brain, president of the Family Planning Association, took the chair.

Experiments five or six years ago, said Dr. Pincus, showed that though the normal function of progesterone was to help pregnancy by ensuring implantation of the ovum, in large and appropriately timed doses it would inhibit ovulation in all species and prevent fertilisation. Since injections of progesterone were painful, and oral doses not very effective, allied compounds were sought in the hope of finding one that would be more effective by mouth. Three 19-norsteroids emerged, all especially active in inhibiting ovulation: 'Nor-

lutin,' ' Enovid,' and ' Nilevar '—or compounds I, II, and III respectively. Of these enovid was the most potent inhibitor of fertility in the rat and of ovulation in the rabbit. It had some progestational effect, but less than progesterone, and some œstrogenic effect.

The three compounds were tested for their effect in inhibiting ovulation in women—first in volunteers, giving one 10 mg. tablet daily from the 5th to 24th days of the menstrual cycle, then in patients in a mental hospital. The indices of ovulation used were: (1) the peak of temperature; (2) vaginal smears; (3) endometrial biopsy; and (4) urine output of pregnanediol. In the volunteers, with compound I, the mean length of the menstrual cycle was unchanged, evidence for ovulation was lacking in 76% of cycles by endometrial biopsy and in 92% by other tests, and pregnanediol excretion fell to a tenth of normal. At laparotomy in 12 women, no evidence was found of recent ovulation. When treatment was stopped, normal cycles were resumed, though the first was delayed. The findings with compounds II and III were similar. In the mental-hospital patients, there was some shortening of the cycle with compound I, but not II. The plasma-free corticoids were increased or unchanged, and the plasma-bound corticoids decreased. With compound II, there was diminished excretion of corticosteroids, pregnanediol, and gonadotrophin.

A field trial was then begun, in cooperation with the Family Planning Association of Puerto Rico, to test the contraceptive effects of enovid. Women were given tablets and told to take one daily from the 5th to the 24th day of the cycle, and were visited monthly by social workers who asked them how many tablets they had in fact taken; if they had missed any they were advised to go on till they had taken all twenty. 70% of the women took the tablets daily as prescribed; in these the cycle length was normal, with a less wide range of lengths than is found in untreated women; in those who missed one to five tablets the cycle tended to be shorter or longer than normal, and in those who missed more than five the cycle tended to be longer. The output of corticosteroids in the urine was decreased; the hæmoglobin and clotting-time remained the same, and the bleeding-time became a little shorter. The menstrual flow seemed unchanged but there was a tendency for dysmenorrhœa to be relieved. Endometrial biopsies revealed much the same picture throughout the cycle—that typical of the 19th day normally—and œdema of the stroma. 14% of the women had side-reactions, such as nausea and abdominal pain, which were sometimes severe enough to cause them to abandon their tablets, but which were relieved by antacids in 90%, and by a placebo in 65%, of cases. The effectiveness of the drug as a contraceptive is shown by these figures:

| | *No. of tablets missed* | *No. of pregnancies (per 100 woman-years)* | |
|---|---|---|---|
| *Untreated* | .. | 62·5 ± 1·35 | |
| *Treated:* | | | |
| | 0 | 0 | 3·8 |
| | 1-5 | 9·2 | |
| | 6-19 | 25·9 | |

Dr. Pincus concluded that enovid, by virtue of its action in inducing a premature luteal phase, is an effective contraceptive; and most women are happy taking it. The problem in Puerto Rico is to find enough of it to satisfy the demand.

# The Widdicombe File

## XLV. CAROLINE'S FUTURE

MY DEAR RICHARD,

How *thoughtful* of you to send me your Uncle Tom's letter!* And how nice to see that he is still the same dear little boy I remember so well—perhaps a little younger, but then time does fly so, doesn't it? And what a coincidence that it should arrive just at a time when we are all so *preoccupied* with our granddaughter Carrie's future. I do so vividly remember dear Noel sitting beside Jeremy and me on the beach in Capri (or was it the terrace in Naples?) and giving us the most wonderful advice about Sylvia. That was Carrie's mother, of course. And I wish I could remember what exactly his advice was: but I know that it had something to do with her going on the stage. And that really was many years before she went to America with Jim (her first) and started to collect those quaint little ottos (or are they oscars?) which now clutter up the house so badly.

Well, poor Noel cannot afford to live in England any longer; so there was *nobody* to tell me what to do with Carrie until you sent me Tom's letter. And I was just about to give her all the *wrong* advice! Because I *did* have misgivings about her wanting to do Medicine. Such a noble profession, of course! But I *never* realised what a dreadful state it had got into and that you needed young women so badly. Not until I read Tom's letter. It used to be so different when I was young. Why, I remember that *all* my doctor friends used to be intense about their work: and I cannot remember *one* who wanted to play with first-stage rockets (whatever *they* are) instead of looking after his patients. But I am sure that's all because today the poor boys are " dragged " and " pushed " and " bullied " and even " *cheated* " into the profession, instead of being allowed to stay at home. No wonder they become such bad doctors. But my dear Richard, you really must put poor Tom's mind at rest. There is still Carrie, and some of her friends, who really *want* to do Medicine: and you cannot imagine how wonderfully intense they feel about it: and with so many lives entrusted to them, let us hope that they always will do. (And surely there must be a *few* young men left like that!)

But then, I must confess to you, there *was* also this question of marriage that kept worrying me. Not that Carrie ever consults me or Sylvia about things like that: but watching our own Dr. Misgust, who comes to write up Jeremy for his sleeping-pills, I did become quite perturbed. Because the poor man is always so terribly bad-tempered: never a moment even to sit down, though he is really wonderfully kind and insists on sending us to the very best hospitals even when it's only a sore throat. And when he did come to tea the other day I felt *so* sorry for his poor dear wife; because I am sure that she wasn't nearly so interested in cancer and yellow fever as Jeremy and I and the Vicar and Mrs. Appleby: and they do have tea together quite often. But I see now how different it will be for Carrie. After all, it *is* quite likely that she will marry a doctor: and then, as Tom says, she and her husband will be able to forget about their marriage now and then and talk " shop ". And when I think of all my friends and their husbands who have had *nothing* to talk about for the last thirty years, and when I have to listen to Jeremy who still talks tinned fruit (although it's five years now since he retired) every time I want to talk to him about something *interesting*, well, isn't it going to be fun for Carrie and her husband to talk the *same* " shop " to each other any time they feel like talking? But, of course, Carrie might not marry a doctor . . . only why does Tom say that if she didn't, it would have to be a poor half-wit? Not that I think that all husbands need to be intelligent, or even bright: but it is really distressing to think that there are only a few Englishmen left who are able to grasp that being a doctor one cannot *help* learning

* Reproduced in the Widdicombe File, March 1.

something about Medicine. (Even those poor bullied young men couldn't help that.) But if things really *are* as bad as all that, how fortunate for Carrie that she will be able to pick one of the few, and that she will recognise the others in time—because superficially most of them appear quite *normal*. And, of course, if she *did* marry a foreigner, like Louis (Sylvia's second) or Adam (her fourth), then it wouldn't matter any longer if he was a bit more or a bit less mad, because, I suppose, there would be other things.

Well, whether one marries a doctor or not, Tom is so right in saying that a husband shouldn't be "just something handy around the house", as most husbands are nowadays. And how nice that Carrie's husband will never have to be just that: because, with other things on her mind, he could almost *run* the house (with a little supervision at first): and wouldn't that be fun for him, and, I'm sure, so much better for the house too?

And thinking of husbands made me think of children: because, however intense Carrie might feel about her Medicine and about her husband, in this modern world a double life like that will hardly be enough to keep an intelligent young woman like her fully occupied. So she will have plenty of children. And when I read in Tom's letter about all the *horrible* brainwashing and bullying that goes on in the schools, I thought to myself that we really must make quite sure that at least they have a nice and interesting homelife. And if Caroline can go out to work and relax, and doesn't have to stay at home and just look after the children day after day after day, and year after year after year, and get grumpier and grumpier, and wearier and wearier, and duller and older all the time, well, then that won't be too difficult. Of course, Jeremy and I, and Sylvia and Ron (her present and fifth), and even perhaps her husband's parents and grandparents will all have to give her a hand: but won't it be fun for the children to have a real *family* about, and not just a lot of old relatives like most other children. And you cannot imagine, my dear Richard, how much we are all looking forward to that: because I don't think you young doctors realise that, now that you keep us old people so wonderfully fit, doing nothing does get a little monotonous. And though I may not have been much good at educating my own children, I did always take the best advice (like Noel's and Tom's); and I did always try to learn by watching other children whose parents did a lot of educating. (And that wasn't usually difficult, because they always came to our house whenever they could get away from their own homes.)

Well, when I told Carrie all this, she said that, though it was a *great* help to get all this encouragement from such an experienced person as Tom, not all doctors were as tolerant and farsighted as he; and that some were positively *obtuse* and didn't like the *idea* of what they called "female competition". So I made a point of asking our Dr. Misgust next time he came: and he got so excited that he spent a full five minutes (which he could have spent examining his next three patients) telling me that women were all right to look after women, but that they just didn't *understand* men. And I said that was exactly what I thought would make doctoring so nice for Caroline: because men, who do understand men, don't seem to care for them a bit: and it must be so much nicer to look after patients one likes. And that made Dr. Misgust quite angry at first (because he hadn't thought of it before): and he said that it showed how illogical women were. (But, of course, women are much more logical than men: because when they do something for the sake of logic they usually have a good reason of their own as well.) In the end he cheered up quite a bit: and before he left he had to admit that Medicine hasn't been the same since women were first allowed to qualify. And when I began to think of all the wonderful discoveries doctors have made since then (even if not *all* were women) I really felt quite proud.

After this all that kept worrying me was the bit in Tom's letter about filling in forms and "dashing to the four corners of the Realm" to try and find a vacancy. But there again, I said to myself, with all those great universities and hospitals absolutely packed with men, and men being so logical, it couldn't be as bad as all that. And it wasn't. Because last week Jeremy went to see Sir Harold Vymme in Harley Street for his quarterly blood-pressure: and after he had had it all checked and adjusted I told Sir Harold about Carrie wanting to study Medicine at St. Nicholas' (which is practically run by Sir Harold's secretary). Well, at first he wasn't a bit hopeful: and I must confess to you, my dear Richard, that when he started telling us in his wonderfully melancholy voice about all the poor young men who wanted to get in, and about them having to earn a living later on, and about having only one vacancy for three, and whether I thought it fair to keep one of them out to get Carrie in . . . well, I suddenly felt quite ashamed of myself. And I said I would call in Carrie and put it all to her in this way; and that I was sure that when I had done that, she would want to change her mind. And so I did call in Carrie: but it wasn't Carrie who changed her mind. It was Sir Harold. Because just as I was coming to the bit about those nice young men wanting to get in (and the tears began to roll down Carrie's cheeks) Sir Harold suddenly remembered that it was just remotely possible that he may have forgotten about one particular vacancy. And that brought just the faintest little smile to Carrie's face: and I know it's not for me to say, but she really does look *so* pretty every time she does that. Her mouth opens just a tiny bit and . . . but I mustn't stray from what I was saying. Or rather, I wasn't saying very much by then; because the more Sir Harold thought about it, the more sure he seemed that there was, in fact, a place still open. But of course he was quite firm with Carrie: and he said that she would have to come and see him in his office first. And Carrie said that she would love to go, even if there was not the slightest chance of her staying on. But by then Sir Harold was quite positive that there would be. And Tom really mustn't be too unfair on men (even if they are only logical most of the time); because this only happened last week and today Carrie telephoned and said that it was all arranged for her to start at St. Nicholas' next autumn. And whatever happens, my dear Richard, you really *mustn't* let Tom chain himself to the Palace railings. That was all right with only a king living there, but now that even *that* job has to be done by a young woman, it really wouldn't be fair. But do thank him again for all his wonderful encouragement: and I am letting Mrs. Appleby and all my friends read his letter so that they can all benefit from his advice.

Goodbye for now, my dear Richard, and give my love to all the family.

Your affectionate old friend,

MARY WORTHINGTON.

# Conferences

## HORMONES AND ATHEROSCLEROSIS

A CONFERENCE sponsored by the endocrinology and heart sections of the National Institutes of Health was held from March 11 to 14 at Brighton, Utah, under the general chairmanship of Dr. GREGORY PINCUS (Worcester, Mass.).

### Cholesterol Metabolism

Prof. SUNE BERGSTRÖM (Lund), who considered the influence of intestinal flora on the excretion of cholesterol and bile acid, showed that hypothyroid rats excrete almost pure cholic acid, whereas hyperthyroid rats excrete mostly chenodeoxycholic acid. This difference may be due to stimulation of bacterial floral activity by the thyroid hormones. He agreed that, although the liver is the primary site for cholesterol degradation, all tissues have the capacity to degrade cholesterol into bile acid.

Dr. G. S. BOYD (Edinburgh) showed that in rats thiouracil has an extrathyroidal effect in elevating plasma-cholesterol. Triiodothyronine and tri- and tetra-iodothyroacetic acids cause selective increase of the oxygen requirements of isolated myocardium, and the administration of tri-iodothyroacetic acid to hypercholesterolæmic rats reduces both plasma-cholesterol and lipid deposition in the aorta.

Dr. J. E. RALL (Bethesda) demonstrated that low concentrations of circulating thyroxine are bound between the alpha-1- and alpha-2-globulin fractions, but that higher concentrations are apparently attached to albumin. Sex hormones can influence thyroid activity by altering the protein-binding capacity and thus altering the concentration of circulating free thyroxine.

### Arterial Wall and Cholesterol Transport

No critical level of blood-cholesterol has been observed for the development of experimental atheroma, and hypercholesterolæmia induced by alloxan or detergents is not often followed by atheromatous lesions; these observations, and the irregular distribution of atheromatous lesions, do not accord well, in the opinion of Dr. R. L. HOLMAN (New Orleans), with the filtration theory of the pathogenesis of atheroma. He emphasised the importance of the arterial wall, indicating that atherosclerosis is a gradually progressive process with well-defined histological stages.

Dr. N. T. WERTHESSEN (San Antonio) showed that the accumulation of cholesterol in the isolated perfused aorta is directly related to the initial concentration of cholesterol and to the glucose content of the aorta.

Dr. D. B. ZILVERSMIT (Memphis) has shown by tracer studies that all phospholipids have a higher specific activity in the aorta than in the plasma. He believes that excess phosphatide in the aorta is probably due to local synthesis. It is possible that once the process of arterial lipogenesis is set into motion, reduction of hypercholesterolæmia will have little effect.

Dr. LEON HELLMAN (New York), who has cannulated the left thoracic duct in humans, reported the results of simultaneous analyses of the plasma and lymphatic lipids. In normal people and in hypercholesterolæmic non-lipæmic patients, the plasma specific activity of $^{14}C$-labelled free cholesterol is greater than that of esterified cholesterol, but in hypercholesterolæmic hyperlipæmic subjects the specific activity of $^{14}C$-labelled ester cholesterol is greater. This might suggest the possibility of a defect at the intestinal level of absorption. Dr. Hellman indicated that the fall in plasma-cholesterol following corn-oil administration is more directly related to excretion of sterols than to that of bile acids.

### Hormones and Experimental Atherosclerosis

Dr. DAVID ADLERSBERG (New York) showed that cortisone and prednisone increase plasma-free-cholesterol, beta-lipoprotein cholesterol, and plasma-phospholipids. The combination of cortisone with cholesterol feeding causes greater hypercholesterolæmia but less atherosclerosis in animals fed cholesterol alone. He suggested that this may be due to a decrease in arterial permeability produced by cortisone, and in support of this the simultaneous administration of hyaluronidase increased the degree of atherosclerosis.

Dr. S. O. BYERS (San Francisco) reported that rats which were intermittently stressed by contact with an electrical charge at varying points in their cages, and were therefore very active physically, had no change in the plasma cholesterol or phospholipids, but had shortened clotting-times when compared with a control group.

Dr. MARMORSTON (Los Angeles) reported that in dogs a single injection of corticotrophin (A.C.T.H.) resulted subsequently in a greater hypercholesterolæmic response to cholesterol and thiouracil feeding than if no corticotrophin had been administered. Extensive atheroma developed in these dogs throughout the vascular tree and some even had cerebral hæmorrhage. A flaccid paralysis was observed in other dogs, but it was not clear whether this was related to the cerebrovascular lesions.

Dr. R. PICK (Chicago) believes that a decrease in the cholesterol/phospholipid ratio is more closely related to the experimental regression of atherosclerotic lesions in the chick than any other lipid measurement. All her experimental observations on the chick have emphasised that the aorta is more sensitive to the production and reduction of lipid-rich lesions than the coronary arteries.

Dr. R. H. FURMAN (Oklahoma City) reported a case of biliary cirrhosis in a woman, aged 30, in whom the plasma-cholesterol increased to 3000 mg. per 100 ml. but the cholesterol/phospholipid ratio remained less than unity. At necropsy there was atherosclerosis in the aorta but the coronary arteries were healthy.

### Hormones and the Blood Lipids

Dr. JOSEPH SEIFTER (Philadelphia) reported further studies on a lipid-mobilising factor that can be demonstrated in the posterior pituitary of hogs and is apparently independent of known pituitary hormones. Parenteral injection of lipid-mobilising factor produces hyperlipæmia in the systemic circulation in the presence of liver damage, but with a healthy liver this hyperlipæmia is confined to the portal circulation.

Dr. R. H. ROSEMAN (San Francisco) reported that the plasma-cholesterol levels were increased and that the clotting-times were decreased in accountants when they were undergoing the stress of having to balance quarterly accounts.

Dr. DAVID ADLERSBERG (New York) emphasised the association of acute pancreatitis with hyperlipæmia and felt that the role of glucagon in the regulation of lipid metabolism needed considerable clarification. Dr. G. S. BOYD (Edinburgh) did not observe destruction of the alpha-cells following cobalt chloride administration, which resulted in a rise in the plasma-cholesterol and a fatty liver in his rabbits. Dr. E. STRISOWER (Berkeley) reported that the concentration of high density lipoproteins decreased after the administration of very large doses of desiccated thyroid, thyroxine, and triiodothyronine to euthyroid patients. Dr. M. F. OLIVER (Edinburgh) had also observed a decrease in the alpha-lipoprotein concentration with large doses of thyroxine and triiodothyronine, but he felt that this might be a dose effect since the alpha-lipoprotein level was actually increased with smaller doses of these thyroid hormones.

Dr. HOWARD EDER (New York) reported that a low dose of methyl testosterone did not necessarily produce much change in the total cholesterol in the plasma, although the beta/alpha-lipoprotein ratio is increased. Similarly, he had observed a decrease in the beta/alpha-lipoprotein ratio without any very significant change in plasma-total-cholesterol following the

administration of certain weak œstrogens. He raised the question whether a compound which allowed a change in the lipoprotein ratio but not in total cholesterol was of any value in influencing atherosclerosis.

### Clinical Biological Relationship

Dr. A. R. P. WALKER (Johannesburg) emphasised the rarity of coronary-artery disease in the Bantu. Cerebral atherosclerosis and hypertension are common and often severe. The principal differences from Western nations are in the diet and physical activity. There is a higher concentration of unesterified fatty acids, greater fibrinolytic activity, and greater œstrogen excretion in the Bantu than in the White. A third of adult male Bantus had gynæcomastia, but as yet there is no definite correlation with the incidence of liver disease. Liver disease probably contributes to the rarity of atherosclerosis in the Bantu, but this is probably mostly determined by the diet.

Dr. M. F. OLIVER (Edinburgh) indicated that various thyroid analogues decreased the plasma-cholesterol without apparently increasing the basal metabolic rate, but so far these had proved to be unsuitable since the cholesterol-lowering effect could not be maintained beyond a few weeks and angina was aggravated in a quarter of his patients. Following the clinical trial of several weak œstrogens, he concluded that it was not yet possible to dissociate the cholesterol-lowering action from their feminising effects. (Dr. ROGER ROBINSON [Worcester, Mass.] and Dr. VICTOR DRILL [Chicago] had found the same.) Although the administration of ethinyl œstradiol for two and a half years to 50 men with myocardial infarction had reduced the plasma-lipid levels, there was no difference in morbidity and mortality from further coronary episodes between these men and another 50 receiving lactose.

Dr. J. STAMLER (Chicago) reported similar results from a group of about 100 men who had received 'Premarin' (conjugated œstrogens) over a three-year period. There was no definite evidence, therefore, that the long-continued reduction of the plasma-lipids improved the prognosis.

## NEOPLASIA

A CONFERENCE on Neoplasia organised by the post-graduate medical education committee of the University of Glasgow and the Royal Faculty of Physicians and Surgeons was held on March 26–28.

### General Concepts

Dr. PHILIP PEACOCK said that the first rational idea of causation was Percival Pott's observations on chimney-sweeps' cancer of the scrotum. Tumours arise in all animals, but some tumours common in man seem to be rare in other animals. Theoretically cancer can start from one cell, but the earliest case which Dr. Peacock has seen was multicentric. In this case, in addition to the definite neoplastic foci there were areas of retained sebaceous secretion, and the possibility of this being carcinogenic must be considered, especially in view of recent suggestions that cholesterol is a carcinogen. Perhaps cholesterol can be transformed into methyl cholanthrene. Except in a few industrial cases the cause of carcinoma is unknown; and even where the carcinogen is recognised, the final process remains to be discovered. Contaminants of so-called carcinogens may be the active agents.

Some virus-induced tumours regress spontaneously; the reason for this may be in the hereditary transmission of the tumour, and an additive factor may be involved. Dr. Peacock's concept of neoplasia is that cancer is an alternative mode of existence for a cell which is threatened by death. It may be due to imbalance of cell constituents.

### D.N.A.

Prof. J. N. DAVIDSON reviewed the knowledge of cell substances, notably those of the nucleus. Of these, desoxyribonucleic acid (D.N.A.) is the most important. The amount of D.N.A. in the cell is remarkably constant in different organs except the liver, where it is increased. Many tumour cells have more D.N.A. than normal cells. D.N.A. may actually alter the characteristics of cultures and even of organisms. For example, D.N.A. from a mutant added to a sensitive culture will produce mutant cells in the culture. D.N.A. from phage may alter *Escherichia coli*, to produce further phage.

### Endogenous and Industrial Tumours

Dr. B. D. PULLINGER said that some tumours now considered endogenous may eventually be removed from this group by further research. Squamous carcinoma of the lung may or may not be endogenous, but it seems likely that neoplasia of the scrotum is exogenous, as it occurs mainly in the lower social classes and the agent can probably be washed off. The virus tumours of animals are difficult to classify. Some tumours—notably polyposis coli and retinoblastoma—are hereditary. Some—notably carcinoma of the breast—appear to be familial.

It is impossible to study hereditary tumours in man, because of their irregular breeding; but it may be possible to produce tumours in animals which are highly inbred. The reason for tumour formation may be senescence of the cell or the presence of internal substances which irritate the cell. Recently many mammary tumours have been associated with cholesterol deposits. Cholesterol has caused carcinoma in the bladders of mice. It has recently been shown that carcinoma can be produced locally by the injection of œstrogen.

Dr. A. T. DOIG spoke of industrial cancer. The possible factors involved are tar, pitch, shale-oil, asbestos, X rays, ultraviolet rays, arsenic, and chromates. Radium and radioactive materials have become important. Latent periods may be long. In some industries non-carcinogenic materials may be substituted, and in some the process can be properly screened. Dr. Doig made a strong plea for the notification of all cases of possible industrial cancer, so that the conditions of work might be inspected.

### Reticulo-endothelial System

Dr. R. I. SHAW DUNN classified tumours of lymphoid tissue into (1) Hodgkin's disease, with subdivisions of typical, atypical, Hodgkin's sarcoma, and Brill's disease; (2) lymphosarcoma, which may be small- or large-celled; (3) lymphoreticulosarcoma; (4) reticular cell sarcoma; and (5) miscellaneous.

Dr. A. BROWN dealt with the clinical picture of "reticulosis". Leukæmia is merely a symptom of several different diseases. There has been a gross increase in this condition after atomic bombing, and in radiologists, but its incidence has also increased in the general population over the same period. The prognosis of these diseases of the reticulo-endothelial system is poor, the average survival being two and a half years—though patients with Hodgkin's disease may survive for several years and those with chronic leukæmia for up to twenty years. The management of these lesions is non-specific. X rays may be used at the local site of a disease; chemotherapy is generally reserved for radioresistant or generalised lesions. Dr. Brown favours nitrogen mustard by injection, but recent results with tretamine (T.E.M.) and busulphan ('Myleran') are poor. Anti-metabolites, such as folic-acid antagonists and purine derivatives, are giving some beneficial results.

### Regional Cancer

*Prostate*

Mr. W. B. STIRLING said that in prostatic cancer the serum-acid-phosphatase is increased in 90% of cases. Only 5% of the patients are suitable for radical prostatectomy; the rest are treated by stilbœstrol. Without treatment, the average duration of the disease is fifteen months, with 9% five-year survivals; after stilbœstrol the average duration is forty-five months, with 27% five-year survivals. Adrenalectomy and hypophysectomy yield poor results.

*Liver*

Prof. J. W. ORR (Birmingham) pointed out that, in Africa, primary cancer of the liver is found in 1% of all necropsies, compared with 0·1% in Europe. In South China and in Indonesia it is common in the natives but rare in Europeans. The age and sex distribution is explicable by the survival-rates of these populations. Race seems to have little effect; the Africans in America have lost their tendency to primary liver cancer. This uneven incidence of carcinoma of the liver may be explained by a dietetic deficiency or by a toxic factor. Primary liver tumours are not common in animals, but can be induced by butter yellow and similar substances. The tumours that develop are similar to the primary tumours in man. It seems likely that carcinoma develops on a process of regeneration.

*Stomach*

Prof. C. F. W. ILLINGWORTH remarked on the poor results of the treatment of carcinoma of the stomach—a disease which now causes the death of 300 people a week in the United Kingdom. The five-year survival-rate is only 2·7% in all diagnosed cases, and 12% in those who have had gastric resection. The ætiology is unknown, and tumours cannot be produced in animals by feeding carcinogens. It is unlikely that gastric ulcers lead to cancer in more than 5% of cases of ulcer. In treatment radical total gastrectomy is unsatisfactory, and partial gastrectomy is probably best. Exfoliative cytology does not add many to the cases diagnosed by other means. Routine test of the stool for occult blood may be a useful screening-test for gastric cancer.

*Thyroid*

Dr. E. M. MCGIRR said that cancer of the thyroid gland accounted for only 0·4% of deaths from malignant disease. At all ages it affects females more than males. There are three main types: (1) differentiated (papillary follicular, and Hurthl-cell adenocarcinoma); (2) non-differentiated; and (3) miscellaneous. Surgery has not given very good results, and radioactive iodine is suitable for only 10% of the cases.

## FREEZING AND DRYING

THE second international symposium on freezing and drying was held, under the auspices of the Institute of Biology, in London on April 1 and 2.

### General Topics

Dr. H. T. MERYMAN (U.S.A.) discussed the mechanical and biochemical changes during freezing in biological systems. He felt that a balance must be reached between rapid cooling (in which mechanical damage is maximal) and slow cooling (in which biochemical damage is maximal). The use of additives, such as glycerin, may be rendered unnecessary by uniformity in freezing and thawing.

The paper by Prof. N. KALABUKHOV (U.S.S.R.) was read by Dr. A. U. Smith. It dealt with the problems of undercooling, freezing, and vitrifying whole animals. Experiments were described in which bats were undercooled to −5 to −7°C, and survived storage at these temperatures for periods up to several days. At −4·3°C the heart-rate of bats was about 8 beats a minute, compared with the normal rate of 400.

### Microorganisms

Dr. W. J. SCOTT (Australia) discussed the role of protective agents in storing freeze-dried bacteria. One cause of death is the intracellular reaction of carbonyl with amino groups—known as the browning reaction. This occurs in dried preparations, and the water formed during the reaction accelerates the process. Glucose or ribose in the medium improves the viable count immediately after freeze-drying, but exerts a deleterious effect on stored organisms. Their corresponding reduction compounds (sorbitol and ribitol) give protection without facilitating the browning reaction. Addition of aminoacids to the freezing-mixtures to compete for the carbonyl groups is another means of protection, Lysine and sodium glutamate have been found useful in this respect. Along similar lines sulphur dioxide, which reacts with ketone and aldehyde groups, exerts a protective action.

Dr. R. I. N. GREAVES described some factors which influence the stability of freeze-dried cultures, with particular reference to the browning reaction. Dried cultures have been boiled to assess the effects of various drying media on their stability when stored for long periods. Glucose in the medium gives high initial survival-rates, but the dried cultures are very heat-sensitive. The greatest resistance to high temperatures was found in media consisting of 5% sodium glutamate in 5% dextran solution.

Prof. D. GRIEFF (U.S.A.) talked of the effects of freezing, low-temperature storage, and drying by vacuum sublimation on the activities of viruses and cellular particulates. Viruses showed less loss of infectivity when they were dried from the vitreous, rather than the crystalline, state. The activity of mitochondria, measured by their capacity for oxidative phosphorylation, was better retained after slow than after rapid freezing. This is possibly related to the preservation of the integrity of mitochondrial membranes.

Miss B. L. BRADY described observations on the freeze-drying of yeasts, which is used as an ancillary method to maintain the national collection of yeast cultures. With freeze-drying little difference is noted between the survival-rates of sporing and of non-sporing cells, and between haploid and diploid organisms. There are generic differences in survival-rates. After freeze-drying no change has been noted in vitamin and aminoacid requirements of the yeasts.

### Grafts

Commander G. W. HYATT (U.S.A.) spoke of experience in maintaining a bank of freeze-dried human cadaveric tissues for use in surgery. Skin, dura, fascia, bone, and arteries are removed aseptically from selected sites. The tissues are placed in a medium containing serum and then freeze-dried at 4°C for six weeks, at the end of which the moisture content has fallen to 2·7–3·5%. The materials are stored in sealed vessels at room temperature until needed. Bone stored for up to five years has been used successfully.

Prof. C. G. ROB described the experience of his surgical unit with freeze-dried arterial grafts. Of the last 394 arterial reconstructions, 178 were carried out with homologous tissue transplants. Frozen arteries were used in 78 of these, and freeze-dried arteries in 100. The two types of material take equally well. The criterion of success is the absence of thrombosis, and anticoagulant drugs are an essential part of postoperative routine.

Colonel F. HENAFF (France) discussed freeze-drying associated with corneal grafts. The freeze-dried corneas are undoubtedly non-viable, but both full-thickness and lamellar grafts have successfully been carried out with homologous and heterologous (dog) material.

Dr. A. S. PARKES discussed the freeze-drying of viable grafts. Rat ovaries are good test material because when they are grafted they become physiologically active after a few days. Frozen ovaries retain their activity for at least two years when stored in 15% glycerin at −79°C. At this temperature viability has been maintained although the tissues are effectively dry, because their water is in the form of ice. The problems are how to remove the ice, and what to do with the residual glycerin. High concentrations of glycerin are toxic at room temperature. This is therefore an unsuitable component of freeze-drying media. An ideal protective agent would protect against freezing, be non-toxic, and sublimate with ice during the drying process. To this end, methanol has been tested on rat ovarian tissue in freezing experiments. Viable grafts have been obtained after ovaries have been kept for a few hours in methanol at −20°C.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

I SPENT most of Easter in a new way—on a protest march. A new experience for one so apolitical. A most impressive experience. So many sorts and conditions of men, all trudging along in the foul holiday weather to Aldermaston. I couldn't stay the whole course, for family reasons, but managed Good Friday and the Easter Monday march to Aldermaston itself. The skiffle groups and the beards weren't surprising; there were plenty of obvious vegetarian, teetotal, sandal-wearing oddities; but the real surprise was the number of normal, ordinary, shabby people, the kind you see on a bus or in your surgeries, far outnumbering the peculiars. The profession seemed a trifle thinly represented, though I had two medically qualified companions on Friday and one on Monday.

Thirteen miles is a fair stretch, and there were many footsore blistered plodders by the end. An efficient-looking motor-cyclist with a Red Cross flag was in evidence, and I saw one girl with actually bleeding feet waiting for his attention. The organisation was extraordinarily well done and not obtrusive. The marshals wore tangerine armbands and appeared at intervals, shepherding the stragglers and keeping the column more or less in triple file. It seemed endless, winding along over hills and bridges—you could see the big black square banner at the head, but not the tail, just a three-deep switchback of people who felt strongly enough to be there. There was a policeman every 100 yards or so, friendly and smiling, but efficient—a collie, one felt, who would stand no nonsense from his flock but who had their interests at heart. The considerable traffic wasn't allowed to jostle us too closely and often had to wait.

When we got to the precincts of Aldermaston we marched in silence—fairly strictly observed for the most part, though there were some inveterate chatterers behind us. Aldermaston seemed a blend of science fiction and normal life. The high wire, dogs, armed guards, and some very functional buildings all fitted in; but there was a lake, and some blocks of buildings in contemporary colours like modern flats, which looked out of place. We marched round it, silent, a bit grim, tired and cold. There were thousands of spectators; nearly all were friendly, and many, from Trafalgar Square to Aldermaston, smiled and clapped and shouted encouragement. Some of course just "gawped" indifferently, but the overwhelming impression was of support.

The journey home took *hours*, but for all that it was a satisfying way of spending Bank Holiday. Next morning my five-year-old said "Did you stop them?" I couldn't think what he was getting at and said ungrammatically "Stop who?" "The Government," he said, "from making H-bombs." I had to confess we hadn't—yet.

* * *

Some years ago we designed a controlled trial to assess the effect of winter chemoprophylaxis on chronic bronchitics in a community. Only subjects who were severely affected were included and they were given either real or dummy tablets of a certain drug according to the dictates of our statistician.

Last year, when we revisited the community to invite its members to take part in a further investigation, we were dismayed by their apparent reluctance to cooperate with us again. We soon discovered that their hesitation was due to apprehension lest we were about to issue more tablets; for, while we had found the results of the previous trial statistically insignificant, the subjects themselves had carried out their own analysis in the years that followed and come to a highly significant conclusion: almost all who had taken *any* of our tablets were now either very much worse or dead.

* * *

Archie White had been a sore trial to many of us. A young man with a duodenal ulcer, he had fallen in with a gang of car thieves and as a result spent three months in gaol. Unimpressed by this experience he made further unsuccessful excursions into the illicit car trade and again enjoyed Her Majesty's hospitality for a year. Soon afterwards he appeared at my clinic and I sternly warned him that he must mend his ways or he would find himself breaking stones in penal servitude. It was clear that Archie found this prospect unattractive and he promised to abandon his old associates. Later I heard that he had a job with a firm of road contractors.

I saw nothing more of him till last week. Held up in a traffic block I was idly gazing at a group of workmen who were repairing the road when I saw the figure of Archie White bending down to pick up a large cobblestone. He looked up, recognised me immediately, and reaching for a hammer proceeded with a rueful shake of his head to break the stone. As I drove past he favoured me with a splendid wink and a touch of his cap.

* * *

I always enjoyed walking on stilts. Since I reached an age when it no longer seemed normal to possess a pair I have longed for the time when my son would be old enough to own some.

Recently I bought a pair. They were made of red tubular steel and were much more handsome than the home-made ones I had used in my youth. I hid them in the cellar to await his birthday, but I was so excited about them that I found it difficult to keep them there. I admit that once or twice, after he had gone to bed, I fetched them and walked them round the drawing-room. After all, I had to make sure of my superiority before he received them.

Two days before his birthday my son announced that he was so glad he was receiving a clockwork train for his birthday. I remembered in horror that, months before, I had promised him a train. A train there would have to be.

Now the stilts must remain in the cellar until Christmas. I long for them more and more, but will content myself with nocturnal walks on them round the garden on summer evenings. Perhaps it is better so. Toys are best when they are not shared, and I never was enthusiastic about clockwork trains.

* * *

We thought we finally decided to buy the house because it had two gates. We had always hated backing the car into the road and at last we had a drive encircling a green lawn. We kept our gates open and drove in at one and out of the other. But patches of brown appeared on the lawn and ruined its appearance. Investigation disclosed that every passing dog entered one of our gates and left by the other, leaving his mark on the lawn in passing. When, for experimental purposes, we left one gate shut, no dog entered. It had not occurred to us that dogs would share our liking for double gates. Their motives must be purely psychological. A dog does not need to exit in reverse through a single gate.

We decided that our motives were psychological too. We now keep one gate closed and through the other we reverse the car as before. What we really like of course (and this must be the real reason why we bought the house) is looking out of the window on to a green lawn. In that, at least, we differ from the dogs, except our own, who fortunately shares our respect.

* * *

*News from School.*—On Friday there was for me the great event of the term, particularly as there were only four other dinner-jackets there. It was in the gym of a school at ————. It started at 7.30 sharp. At that hour all the males were sitting self-consciously round the walls. At 7.31 the females trooped in, not quite in crocodile, but possibly in height order from the front. After we had sat there for five minutes more, with the mediocre band playing moderately hard, I leaped to my feet, singled out a female on the other side, and gave a demonstration of the Gay Gordons with her. She had only done it once before. After that all the earnest, dark-suited, open-neck-shirted boys surged to their feet as one, and there was a hubbub of intelligent conversation. My partner thought I was a sort of Carruthers and I did not disillusion her. We danced until 9.45, when my house-master had ordered us to start back. By that time I knew her first name, just. She doesn't know mine. I hope that all she will remember is the brilliant conversation, the unobtrusively perfect dancing, and the perfect breeding of the charming young gentleman who whisked her round the floor so effortlessly that March night. She told me her father had forbidden her to rock and roll, so we rocked and rolled. After that we parted, she with a wistful look in her eye.

# Letters to the Editor

## A BALANCED HOSPITAL COMMUNITY

SIR,—A consultant colleague greeted me on the morning of April 5 with the remark, "This man McKeown is talking sense about hospitals". That sentiment will surely be echoed by all who have studied the needs of our hospital service. I write, however, to remind your readers that the views so ably supported by Professor McKeown's figures for Birmingham were one of the basic reasons for introducing a regional and group hospital service. Experts writing as early as 1938 in the prize-winning article on a hospital service, The Walton Plan,[1] made a plea for

"... real general hospitals which will admit all kinds of cases including infectious fevers, tuberculosis, maternity, mental disease, and sick children. The hospital will have 1000 to 1200 beds and serve about 100,000 people. A general hospital of this kind will be able to care for a large number of chronic cases without exhausting the interest of the staff. There is a great tendency to exaggerate the degree of infirmity of those who are merely old ... as under the scheme there will be no acute hospital, so there will be no need for the corollary, the chronic hospital."

This conception became the basis of all discussions on future hospitals, and writing in 1942 in *Health for All* I was able to "make another assumption, that all hospitals in a socialised service will be general hospitals taking every type of case". Indeed one had in mind and has always advocated a system of general district hospitals which would assume the primary responsibility, in the closest cooperation with the general practitioners, for all the hospital and specialist care needed by its unit of population. It could not effectively deal with everything on the spot, but it could take the responsibility for deciding how each case should be dealt with most efficiently (from the sick person's angle) either because it had the resources or could direct the patient to the necessary resources. (This is of course the principle on which our group laboratories which give an open-access service operate, with all the reference laboratories to take the more unusual cases from them.)

In short, the theory of twenty years is shown to be correct by general experience and now by Professor McKeown's excellent article. But why do we seem so far from the ideal? Is it the profession which has not realised this need and so has not put the right pressure on the lay and financial authorities to amalgamate and reorientate our hospitals? Are we still bound by ideas nearly as old as our hospitals (more than half of them one hundred years old) and so unable to advise our lay committees with the authority that would make them move? I hope Professor McKeown's article will set the ball rolling.

Kingston Hospital,
Kingston-upon-Thames, Surrey. D. STARK MURRAY.

## "THESE DYING DISEASES"

SIR,—Dr. Ambrose King's thoughtful article on venereal diseases (March 29) is timely and shows clearly the difficulties which are rapidly approaching in the present venereal-disease service. In spite of Dr. King's rosy picture for the future of this branch of medicine, the hard fact remains that the young man with at least 35 years of active life in front of him obviously does not consider that venereology is for him, and the service as we know it is slowly but inevitably disintegrating. The time has surely come for fundamental reorganisation in order to have a workable scheme ready for the care of these patients when the present system breaks down.

Venereology differs from most other specialised branches of clinical medicine in that it is specialisation in a group of disease processes, whereas other specialists are concerned with all types of illness and alteration of function which may affect the part of the body in which they are particularly interested. The difficulties attendant upon specialisation in a disease have recently been seen with tuberculosis, and the same trend is happening with venereal disease. It is probably this and the relatively small number of new cases seen at each clinic that discourage recruits, rather than such factors as hours of work, &c.

From Dr. King's figures, the majority of the cases attending the clinics are not suffering from venereal disease; the cases with non-specific urethritis are now the major problem, and these are in need of general medical investigation and care. Most cases of late syphilis are treated by the physician specialising in the organ mainly affected and not by the venereologist. In the same way, the treatment of all these patients could be taken over by the appropriate specialist. Patients presenting with skin manifestations could be treated by the dermatologist, congenital infection by the pædiatrician, genitourinary discharge by the genitourinary specialist or the gynæcologist, non-specific urethritis by the general physician, and so on. This is virtually what has happened in the case of tuberculosis.

Two problems remain: one is the patient with a discharge or fear of infection, and the other is preventive measures. With regard to the first, since 1948 everybody in this country should have his own family doctor, and it is to him that the patient should go, being referred by the practitioner if necessary to the appropriate specialist. With regard to the control of venereal disease, notification, with due safeguards for secrecy, could be introduced by appropriate legislation so that control can be undertaken by the department best equipped for doing this—namely, the medical officer of health and his team.

Thus, with the inevitable running down of the venereal disease service, the duties formerly undertaken by the venereologist would gradually pass back into the medical fold and the stigma of "special clinics" and special wards would disappear.

These ideas are put forward not in any spirit derogatory to the present venereologists but as a basis for trying to deal with a problem which must be tackled within the next few years when the number retiring exceeds the number of recruits.

Oxford. H. R. VICKERS.

## CONSULTANT DISTRIBUTION

SIR,—It is true, as Dr. Joules says (April 5), that facts are gradually emerging which tend to show some inequity of consultant distribution in the country. It is not true, as Dr. Joules imputes, that the medical profession has failed to strive for an increase in consultant establishments. Indeed, even in Dr. Joules' own region (which, according to details given on p. 748 of your same issue, must be one of the most heavily staffed in the country), there has been considerable agitation in the medical committee to secure a review of the consultant establishment.

It seems that one of the objects of Dr. Joules' letter is to imply that those boards with the lowest consultant staffing ratio may have been influenced by "very powerful medical advisory committees". The figures given in Dr. Joules' letter and in your summary of a written reply by the Minister of Health on March 21 are too sparse for any proper conclusions to be drawn. For example, the table you publish makes no mention of the teaching hospital beds in the various regions, nor does it give a true idea of the number of consultant sessions in each region. Furthermore, we are given

1. *Med. Today*, 1939, **2**, 2.

no idea of the numbers of chronic sick beds (which show considerable variation) in the different regions, or of the S.H.M.O. establishment.

These and many other statistical details will need to be collected before we can draw any valid conclusions about the opportunities for expansion in the various regions. I am, however, heartened by the fact that the figures thus far available suggest that the consultants and specialists committees have been correct in their contention that an increase in senior staffing of the hospital service is necessary.

There is one important aspect of this problem on which we require much fuller information. Whilst the Parliamentary answers reported in *The Lancet* give scanty information about the present staffing ratios of different regions, they give absolutely no information at all about the state of affairs at the inception of the National Health Service. Is the apparently better staffing in certain areas attributable to the efforts of their regional boards since the appointed day, or is it wholly or largely due to such areas having inherited a number of hospitals which were well staffed before the N.H.S.? Further research may show that there has been a (relatively) greater increase in consultant establishments in the apparently worse-staffed areas. On the other hand, it may be true that an area which began with a lower staffing ratio and bed/population ratio has, by virtue of its poor start, been handicapped in its endeavours to secure a bigger slice of the N.H.S. cake.

These are but a few of the many questions which occur to those medical men who seek fuller information on this extremely important subject. The questions published by the chairman of the North West Metropolitan Regional Hospital Board (Jan. 25, p. 220), and which still remain unanswered, were framed with the object of elucidating this vexatious problem.

Radlett, Herts. REGINALD S. MURLEY.

## THE COMMON COLD

SIR,—Dr. Ritchie's articles (March 22) have interested me greatly. I am convinced he is right in his thesis that the toxic manifestations of the common cold are caused by the enhanced virulence of the normal saprophytic flora of the pharynx. I have reached an identical conclusion on the strength of experiences gathered from incidental treatment of a relatively small number of cases of common cold over the past two or three years.

But you rightly point out in your annotation that there are risks involved in building up resistant strains by a widespread use of antibiotics. Your readers may therefore be interested in knowing that results closely resembling Dr. Ritchie's can be achieved without resort to antibiotics. I have used for the resolution of the pharyngeal infection lozenges containing dequalinium chloride, which is a chemical agent active against a wide range of bacteria. On some occasions a combination of this with lozenges containing chlorhexidine dihydrochloride proved more effective. As indication for the systematic use of these compounds I regarded not only the developed sore throat but also dryness in the throat, the presence of which often remains unnoticed even by an observant sufferer.

On two points I am inclined to differ from Dr. Ritchie.

One concerns the question of the virus. The role and the behaviour of the virus is certainly no part of clinical observation. The notion of the virus in common cold is derived from experimental work and has not yet been confirmed by laboratory techniques. It seems to me that, within Dr. Ritchie's thesis, the positing of the virus as the primary factor in common cold is before all else a conceptual device designed to account for the lowering of the body's resistance to its own bacterial flora, setting the stage for the unfolding of the clinical phenomenon, common cold.

But epidemiological observations, such as van Loghem's in Holland, immunological considerations, and observations paying attention to psychological settings in which common cold occurs, or tends not to occur, all are somewhat difficult to reconcile with the virus ætiology of the common cold. Certainly from the therapeutic point of view, in procedures such as Dr. Ritchie's and my own, the virus may entirely be left out of account. It is most impressive to observe how agents that are not known to affect a virus are capable of disposing of a developing cold within the shortest space of time, even within less than 24 hours, restoring the patient to full health. If there be a virus, it behaves as if it did not exist.

The other point is that Dr. Ritchie regards as the second stage in the developing of the illness an attack by the nasal and pharyngeal flora. My observation is that happenings on the nasal mucosa in common cold are distinct from those in the pharynx, and that only the pharyngeal flora is concerned in the attack.

I hope later to set out my observations in some more detail and to propose an alternative theory to that of the virus ætiology of the common cold.

London, W.1. JOSEPH ZELMANOWITS.

## SMOKING AND PEPTIC ULCER

SIR,—The following figures may be of interest in relation to the paper by Dr. Doll and his colleagues (March 29). I quoted them at the recent symposium on carcinoma of the lung arranged by the N.A.P.T.

In a series of 7500 cases of peptic ulcer collected over a period of nearly ten years in the impaired lives registry of the Prudential Assurance Company, so far there have been 45 deaths certified as due to carcinoma; 18 of them were due to carcinoma of the bronchus, 17 to carcinoma of the stomach, and 10 to carcinoma in other situations. This high incidence of carcinoma is not apparent in any other group of impaired lives.

Since smoking has been suspected as a cause of carcinoma, both of the stomach and the bronchus, I feel that these figures, which I quoted by permission of the management of the Prudential Assurance Company, may be significant.

London, W.1. E. H. HUDSON.

## ANOTHER "UNIVERSAL DIAGNOSTIC TEST"?

SIR,—I was very interested to read (April 5, p. 749) about the work at the Johns Hopkins University School of Public Health on serum-mucoproteins.

In diagnostic work of protein paper electrophoresis, we have certainly come to rely on the mucoprotein stain (P.A.S. technique) to quite a considerable extent, since it is the most sensitive and easiest method of demonstrating what I have called tissue necrosis and regeneration.[1] For the past four years the routine strips at this laboratory have been divided longitudinally into three, and a third stained respectively for total protein, mucoprotein, and lipoprotein. The degree of tissue breakdown and repair (e.g., in infections and trauma) is related to the intensity of the alpha-mucoprotein bands.

I have associated tissue necrosis or degeneration with increase or emphasis of alpha-one-mucoprotein, and tissue growth or regeneration with increased alpha-two-mucoprotein. The prognosis in many diseases seems to be related to an alteration in the ratio between alpha-one- and alpha-two-mucoproteins. A prominent alpha-one-mucoprotein band carries a bad prognosis. Alpha-one-mucoprotein is emphasised in many cases of hæmolytic diseases, heart-failure, steatorrhœa, malignant hypertension, some malignant diseases, some virus diseases, &c., and approaching death. Alpha-two-mucoprotein is emphasised in childhood, pregnancy, neoplasia, arthritis, infarction, trauma, and renal disease.

1. Dagnall, P. *Clin. chim. Acta*, 1957, **2**, 381.

The interesting points mentioned in your note are too numerous to discuss here. There are some abnormal beta- and gamma-mucoproteins—e.g., the unusually staining beta-mucoprotein in myxœdema, the gamma-myeloma-mucoproteins, and the mucoproteins of miscellaneous fluids, such as urine and pleural, peritoneal, and synovial fluids.

Rewarding observations may also be made by relating increases in mucoprotein to the appropriate portion of the paper stained for total protein—e.g., in rheumatoid arthritis the increase in alpha-two-mucoprotein is in excess of that shown on the strip stained for total protein. These latter findings may prove to be of greater diagnostic importance than changes in the mucoproteins themselves.

Kingston Hospital,
Kingston-upon-Thames, Surrey. PHYLLIS DAGNALL.

## NEW METHOD OF PHENOBARBITONE ADMINISTRATION

SIR,—I cannot agree that Dr. O'Connor (March 22) has really demonstrated anything.

The mean daily dose of phenobarbitone in the control series was gr. 2·8 daily, and with ' Spansule ' treatment gr. 5·8. The toxic effects noted with the patients receiving regular phenobarbitone were mainly subjective ones, which must be very difficult to evaluate in psychotic patients. It would be reasonable to suppose that such symptoms might disappear if the dose of ordinary phenobarbitone were doubled. This essential control is missing.

Dr. O'Connor must be unaware of the study by Butler et al.[1] These workers showed that in man there was no significant difference in blood levels of phenobarbitone between divided daily doses of regular phenobarbitone and phenobarbitone in spansule form, when equal doses of the active drug were given. For a drug which is excreted as slowly as phenobarbitone blood-concentration variations are slight, and it remains to be proven that they are of clinical importance.

If the missing control experiment were carried out it might be possible to show how worth-while economies could be made in the country's drug bill.

Department of Pharmacology,
School of Medicine,
University of North Carolina,
Chapel Hill, North Carolina. JOHN W. PEARSON.

## MITRAL VALVOTOMY AND PREGNANCY

SIR,—In his comments on our paper of March 15, Dr. Richard Turner (April 5) states that " surgery during pregnancy is undesirable unless the evidence for tight [mitral] stenosis is based on severity of symptoms before pregnancy began." We think this goes too far, for we believe that Dr. Turner underestimates the risk to life when a patient with mitral stenosis develops severe symptoms for the first time *during* pregnancy. Although we agree that pregnancy may magnify the symptoms of mitral stenosis, we believe that valvotomy should be undertaken in at least some of these cases because:

1. The risk of valvotomy during pregnancy is relatively reasonable (2 deaths in 97 cases).

2. The mortality is very high if pulmonary œdema develops during pregnancy (about 40%, unpublished data) and death does not usually occur in the first attack.

3. When pulmonary œdema has occurred in pregnancy, a further pregnancy is too dangerous unless valvotomy is undertaken.

Valvotomy (like termination of pregnancy) should not be undertaken until the cardiac condition has been adequately treated medically.

We are surprised that Dr. Turner demands " objective signs of long-standing pulmonary hypertension " and " an electrocardiographic pattern of right ventricular hypertrophy " before advising surgery. In our experience such evidence is present in only about a third of patients with tight mitral stenosis, and the majority of these patients are so incapacitated that pregnancy is uncommon.

E. G. WADE
W. F. NICHOLSON
Department of Cardiology, A. MORGAN JONES.
The Royal Infirmary, Manchester.

1. Butler, T. C., Mahaffee, C., Wadell, W. J. *J. Pharmacol.* 1954, **111**, 425.

## TESTING OF STERILISATION METHODS

SIR,—Much misgiving has arisen on the value of testing sterilisation procedures by the use of heat-resistant spores. It is quite easy to isolate from soil and dust aerobic-sporing bacilli which are able to stand up to a great deal of heat, but in our experience the spores rapidly lose this property on subculture. For instance, an aerobic-sporing bacillus isolated from soil resisted being heated in a boiling-water bath for $1^1/_2$ hours, but a subculture of the same organism was destroyed in less than 2 minutes in the same water bath.

The " test spores " issued by the Southern Group Laboratory until recently are killed in 7 minutes at 100°C. Preliminary work by one of us (E. H. B.) has shown that the survival power of spores is dependent on the method of preparing them, and in particular on their water content. Cultures incorporated in linen discs and then freeze-dried are much more resistant to heat than those dried by evaporation in warm air. The freeze-dried preparations have been tested by placing a disc in a capped $^1/_2$ oz. MacCartney bottle and not in an envelope. This produces as closely as possible a " standard " preparation in a " standard " air-pocket, and under these conditions the discs have proved satisfactory.

| Conditions | Maximum internal temperature | *Bacillus subtilis* freeze-dried | *B. subtilis* evaporated | Browne's tubes yellow | Browne's tubes black | Browne's tubes green |
|---|---|---|---|---|---|---|
| Steam 30 min. at 109°C or 5 lb. per sq. in. | 110°C | Not killed | Killed | Amber | Amber | |
| Steam 15 min. at 115°C or 10 lb. per sq. in. | 115°C | Killed | Killed | Green | Nearly green | |
| Steam 20 min. at 115°C or 10 lb. per sq. in. | 116°C | Killed | Killed | Green | Green | |
| Hot air 60 min. at 160°C | 160°C | Killed | Killed | | | Green |

Because of the difficulty of obtaining, and maintaining, a " standard " test strain some pathologists have been relying on Browne's tube, which are supplied in the following forms:

| | |
|---|---|
| For glove sterilisation | yellow spot |
| For dressing sterilisation | black spot |
| For hot-air sterilisation | green spot |

According to Medical Research Council memorandum no. 15 (1955), gloves are satisfactorily sterilised at 109°C or 5 lb. per sq. in. pressure for 30–40 min. Unfortunately, the indicator in Browne's glove tube (yellow spot) will not satisfy these requirements, in that the colour change is often not amber, and certainly not green. Heating to 115°C or 10 lb. per sq. in. pressure for 15 min. satisfactorily converts the red colour to green. This treatment does not damage rubber gloves, and their normal life will not be diminished by this repeated steam treatment.[1]

From the accompanying table it can be seen that freeze-dried spores resist 109°C or 5 lb. per sq. in. pressure for 30 min., but are killed at 115°C or 10 lb. per sq. in. pressure for 15 min.; whereas the evaporated spores are killed in both cases.

We cannot, therefore, rely on the present " sterility test packets." Freeze-dried discs will in future be issued for pathologists to transfer into MacCartney bottles.

1. Howie, J. *Lancet*, 1956, ii, 670.

If double testing is not deemed necessary, the Browne's tubes can be taken as reliable. This confirms the conclusions of Alder and Gillespie.[2]

Group 9 Laboratory, Watford, Herts. HERTA SCHWABACHER
A. J. SALSBURY.
Southern Group Laboratory, London, S.E.13. E. H. BAILEY.

## ARTIFICIAL RESPIRATION WITH THE TUNNICLIFFE BREATHING-JACKET

SIR,—I read with great interest Dr. Spalding's and Dr. Opie's thorough report (March 22) on the Tunnicliffe breathing-jacket. In principle the jacket has seemed an advance on the cuirasse, as they have pointed out. However, since it is more complicated to fit on the patient than the cuirasse, we have only tried it for respiration of three patients who were expected to need more ventilation than the Monaghan or 'Spirashell' cuirasse would provide. On these patients its performance has not come up to expectations.

For the first of these, a boy aged 6 years, the smaller size of jacket proved too bulky. On the second, a man with a collapsed left lower lobe and with a vital capacity of 50 c.cm., it would only produce a tidal air of 190 c.cm. with a pressure of −27 cm. of water. Its performance on the third patient, a woman with a collapsed left lower lobe and a vital capacity of 90 c.cm., was studied more fully, and the following figures were obtained (the tidal air was measured on a special small-volume-recording spirometer):

| | *Positive-pressure machine* | *Tunnicliffe jacket* | | *Spirashell cuirasse* | |
|---|---|---|---|---|---|
| Pressure (cm. water) .. | +15 | −27 | −17 | −27 | −17 |
| Tidal air (c.cm.) .. .. | 410 | 350 | 220 | 350 | 250 |

A small or larger jacket produced lower figures.

Although the Tunnicliffe jacket provided no better ventilation than the spirashell cuirasse, it was preferred by this patient because it was more comfortable, though it restricted arm movements.

These two adult patients were more difficult to ventilate than usual. This was shown by the relatively high pressure needed for correct ventilation by the positive-pressure machine. In such cases we expected that the Tunnicliffe jacket might prove invaluable. The figures above show that this was not so.

Ham Green Hospital, Pill, nr. Bristol. R. V. WALLEY.

## LUNG RESECTION FOR BRONCHIECTASIS

SIR,—I agree with Mr. Shaw (April 5) that your annotation of March 22 gives an unjustifiably gloomy picture of the modern results of resection for bronchiectasis. Surely it is wrong to quote one small series alone as confirmation of the view you had stated previously, when the results of this series, for one reason or another, appear to be greatly inferior to those published by the many other workers in recent years. Certainly lobectomy would seldom be justified if the risks were as great as you suggest, but in fact the operative mortality is probably considerably less than 1% in the best hands.

New bronchiectasis developed in a third of the patients. This is a very high proportion, but the statement means little unless one knows the degree and type of bronchial dilatation, and the severity of the associated infection and symptoms as compared with those present before operation.

It is generally agreed that resection is often followed by some loss of lung function on the same side, but Long et al.[3] showed that this may be compensated for by an increase in function of the other lung and that there may in fact be an increase in the maximum breathing capacity. The mechanical and anatomical changes following resection may be harmful, but possibly not more so than the continued presence of a reservoir of infection with its tendency to local and occasionally distal spread.

The indications for or against surgery in a particular case are sometimes clear cut, but in many a decision is difficult, not because the results of surgery are bad but because the results of both surgery and medical treatment are good.

One of the reasons why it is so difficult to make broad generalisations about the relative merits of the two methods of treatment is that there are few if any published results of long-term medical treatment which can be compared fairly with the many surgical reports.

I suggest, Sir, that an open mind should be kept on this difficult subject and that there is no good evidence on which to condemn resection for bronchiectasis.

Chest Clinic, The Marsden Hospital, Burnley. W. H. HELM

## ADRENOCORTICAL STEROIDS IN MALIGNANT EXOPHTHALMOS

SIR,—We wish to support the plea by Dr. Hoffenberg and Dr. Jackson (March 29) for a further therapeutic trial of adrenocortical steroids in malignant exophthalmos. We are prompted to report our experience with a recent patient.

In May, 1956, a woman, aged 23, had a subtotal thyroidectomy. For the previous seven years she had been increasingly nervous, had noticed excessive perspiration, and had lost 7 lb. in weight. In spite of these symptoms, she preferred hot weather. Following the operation, the nervousness was only slightly improved, and she failed to gain weight.

Slight protrusion of the right eye was first noticed four months before her operation, but later this became more severe, and in October, 1956, a right tarsorrhaphy was performed. Her condition then remained unchanged until November, 1957. She then developed severe continuous frontal headache and pain behind both eyes. The protrusion of the right eye became much more severe, and the left eye also began to protrude. There was a rapid deterioration in vision in both eyes, especially in the right eye.

On admission to the National Hospital on Nov. 21, she had bilateral exophthalmos, more on the right, but no chemosis or conjunctival œdema. Her visual acuity was reduced to counting fingers in the right eye, and to Jaeger (J) 20 in the left. The visual field was full on the left, but the lower half of the right visual field was lost. The right pupil did not react directly to light. Bilateral early papillœdema was present. There was severe restriction of bilateral upward gaze, and of abduction of the right eye. Although she was nervous, there were no signs of thyrotoxicosis.

She was treated immediately with prednisolone 10 mg. t.d.s. and triiodothyronine 10 μg. t.d.s. Because of the lack of improvement, a right orbital decompression was performed on Nov. 23. This unfortunately failed to save the vision of the right eye, which became totally blind. The left eye, however, dramatically improved, and by Dec. 2 her visual acuity had increased from J20 to J2, the papillœdema had subsided, and her external ocular movements were full. Thyroid gr. $^1/_2$ b.d. was substituted for the triiodothyronine, and she was discharged on this drug and on prednisolone 10 mg. t.d.s.

As an outpatient, she continued to take thyroid gr. $^1/_2$ b.d. but the dosage of prednisolone was progressively reduced to 5 mg. daily over a period of one month. The drug was completely withdrawn on Feb. 26. Five days later, she developed mistiness of vision of the left eye, and two days later this became much more severe. She was readmitted on March 5. There had been a considerable increase in the degree of proptosis of the left eye, and her visual acuity was reduced to J10. There was complete loss of the temporal half-field, and the defect also spread to involve most of the lower nasal quadrant. The external ocular movements were full, and the left disc was

2. Alder, V. E., Gillespie, W. A. *J. clin Path.* 1957, **10**, 299.
3. Long, J. H., Norris, C. M., Burnett, W. E., Wester, M. R. *J. thorac. Surg.* 1950, **19**, 477.

normal. The right eye was blind, with optic atrophy and a fixed dilated pupil.

She was immediately started on prednisone 20 mg. t.d.s., and within thirty-six hours there was much improvement. The visual field defect began to shrink, and the visual acuity increased. By March 11, her visual acuity had become normal (J1), and only a minimal peripheral temporal field defect remained. This defect has since disappeared. She has continued to take thyroid gr. $^1/_2$ b.d., but the dosage of prednisone has now been reduced to 10 mg. t.d.s.

This case has proved instructive. Although decompression failed to save the sight of the right eye, the left eye improved after operation and this may have been due to the prednisolone which was being concurrently given. The relapse of the left eye followed five days after stopping prednisolone, and impressive improvement began within thirty-six hours of resuming steroid treatment. Although no firm conclusions can be drawn from a single case, we feel that it is reasonable to attribute this patient's improvement to steroids; at any rate we do not propose to risk withdrawing treatment a second time.

We wish to thank Dr. Denis Brinton for permission to report this case.

The National Hospital for Nervous Diseases, London, W.C.1. R. W. HORNABROOK J. C. LEONARD.

## PRE-ECLAMPTIC TOXÆMIA

SIR,—Dr. Margaret Robinson (Jan. 25) holds that the ingestion of extra sodium chloride in the diet is successful in the prevention of toxæmia of pregnancy; but I believe that her study has many shortcomings. Because of the large circulation which *The Lancet* has to the medical profession of this country, I think that this article is more damaging to prospective mothers and to the information of those concerned with their care than any other piece of literature presented to the obstetrician in the past thirty years.

We have statistically analysed Dr. Robinson's data. We found that they were statistically significant in the overall groups. In the age-groups 0–30 and 30–50, the data were significant where toxæmia was commoner among those on salt-poor diets. The data were significant as regards parity only up to para. 4 but were not significant beyond this parity. The neonatal deaths and the presence of œdema showed statistical significance. On the other hand, there was no statistically significant correlation among the prenatal deaths, antenatal bleeding, and antepartum hæmorrhage. We could not differentiate between antenatal bleeding and antepartum hæmorrhage.

Although statistically significant differences existed between the low-salt and the high-salt group, this does not necessarily mean that the patient was protected against toxæmia because of the high-salt diet just because 70% of the patients on the high-salt diet did not develop a toxæmia according to the definition given in the paper. Some other comparisons might be drawn relative to toxæmia of pregnancy too.

Chesley (personal communication) has shown that there is a statistically significant correlation between the presence of toxæmia of pregnancy and membership of the Baptist Church. We have been able to show a high incidence of toxæmia of pregnancy in underweight patients—but also in those who are overweight. It thus seems that some other variable existed as a third factor in the group of patients reported by Dr. Robinson. In England, where there still exist difficulties in getting satisfactory nutrients, why could not the variable of nutrition account for the differences noted in her series? Also, it is not known whether her patients on the increased salt intake were not in various degrees of salt depletion before the administration of supplemental sodium chloride. It seems as though there was no actual control over the sodium-chloride intake among these patients; they were merely instructed to increase their salt intake. It might be open to some question whether the patients actually complied with the advice offered, and even if they did comply by increasing their intake, they may conceivably have increased it only to a level that would be reached by another group who reduced their sodium-chloride intake.

Even under the strictest metabolic conditions of study in hospital patients, there are difficulties in controlling compliance with rigid regimes. The study was not controlled in a hospital, nor were there any biochemical, weight, or endocrinological investigations.

Department of Obstetrics and Gynecology, School of Medicine, Seattle 5, Washington. RUSSELL R. DE ALVAREZ.

## CARDIAC SYNCOPE AFTER SWALLOWING

SIR,—Concerning Dr. James' interesting paper last week, may I just mention, for the sake of completeness, a case of a similar syndrome which was published by myself and H. Uiberall.[1]

A lady, aged 62, had a characteristic Stokes-Adams syndrome with unconsciousness, after swallowing food or fluids first thing in the morning. The electrocardiogram showed signs of sinus bradycardia and ventricular extrasystoles. During the attack, the pulse-rate dropped from about 80 to 44 and the blood-pressure from 220/100 to below 80/0 mm. Hg. The attacks began soon after a bout of tonsillitis. At the time of the hospital investigation it was possible to produce an attack by touching the left posterior arch of the soft palate. After a severe attack there was a refractory phase for over an hour which could be used for the intake of large amounts of food without provoking further attacks. The left tonsillar region was anæsthetised and radium 100 mg. implanted for 3 hours. The attacks increased in intensity for the next 2 or 3 days. On the 7th day a second application of radium was carried out with renewed intensity of attacks lasting about 7 days. From the 8th day onwards after a second insertion of radium the attacks disappeared, and the patient remained free from attacks for the next $9^1/_2$ months.

London, S.W.1. V. C. MEDVEI.

## INDIRECT BILIRUBINÆMIA

SIR,—The observation by Danoff et al. (*Science*, April 4; *Lancet*, Feb. 8, p. 316) that glucuronic acid and its sodium salt administered to infants with hyperbilirubinæmia resulted in a striking but transient fall in unconjugated bilirubin is of extreme interest to all pædiatricians. In our work with glucuronic acid we have been unable as yet to demonstrate a significant fall in bilirubin level. However, we wish to call attention to the potential hazard in the use of these preparations in view of the fact that physicians may be tempted to substitute glucuronic-acid therapy for replacement transfusions in newborns with dangerously high serum-bilirubin levels. Should the reported findings be confirmed, there is no indication regarding the fate of the declining serum-bilirubin. The possibility has not been excluded that bilirubin is driven from the blood into the tissues, thus increasing the risk of brain damage.

Until further investigative work determines the exact pharmacodynamic action of these compounds we feel strongly that physicians should refrain from using them in the newborn.

Boston City Hospital, Boston 18, Massachusetts, U.S.A. RUDI SCHMID GLORIA JELIU SYDNEY S. GELLIS.

1. Medvei, V. C., Uiberall, H. *Wien. klin. Wschr*, 1938, **51**, 234.

## THE DOCTOR'S ATTITUDE TO HIS PATIENT

SIR,—Because Dr. Ryle (April 12) is the fortunate possessor of such characteristics that he can adequately treat his patients he should not decry the endeavours of us others to understand our patients better, or deny that we others do need to suffer a change before that can happen.

I am sure "we" are in the majority: otherwise, would there be so many "doctor satellites" revolving, as hopelessly as "Laika", around our surgeries?

We all suffer a "sea-change" in the depths of our personalities by constant contact with those around us, but the change into something richer and more understanding is quicker in the greater awareness of a seminar such as Dr. Michael Balint's.

Dr. Ryle and Dr. Tuckman (March 29) have evidently had no such experience. For my own I shall always be grateful.

Ilford, Essex. R. N. COMPTON SMITH.

## A SLIDE-HOLDER FOR STANDARD FILING CABINETS

SIR,—The problem of storing a large number of lantern slides or dental radiographs compactly and yet in a way which makes them readily available for inspection and selection may be solved by the construction of slide-holders in the following way:

Strips of transparent polyvinyl chloride (P.V.C.) ($1^3/_4$ in. × $14^1/_2$ in.) are welded on to a sheet of natural P.V.C. ($10^1/_2$ in. × $14^1/_2$ in.) to form twenty-four pockets, each holding one 2 in. × 2 in. slide (fig. 1). Welding is by radio frequency.

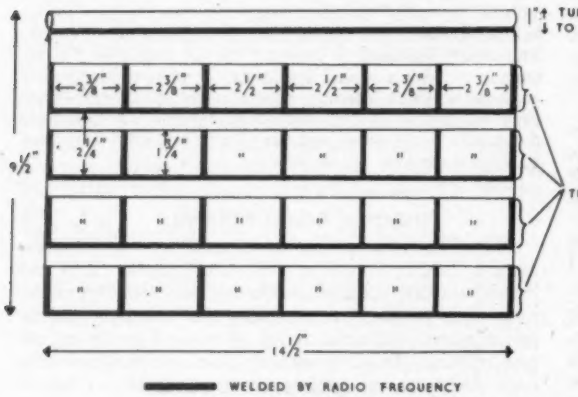



Fig. 1—Dimensions of slide-holder.

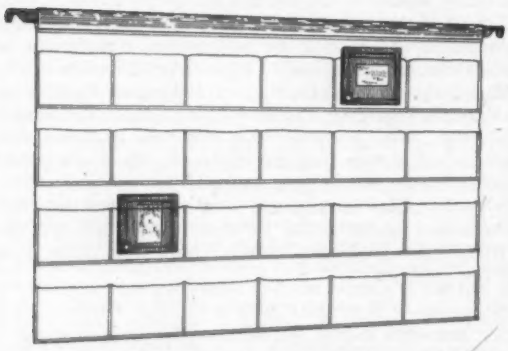


Fig. 2—Slide-holder complete.

At the top of the frame a loop is made to hold a standard filing-cabinet metal bar (fig. 2). The frame can then be placed in a filing-cabinet drawer, each drawer holding about 100 frames, or 2400 slides. For catalogue marking or indexing a typed card can be slid in the loop holding the metal bar; typescript can be seen through the translucent P.V.C.

All the slides in a frame may be viewed by holding the frame up to window light (the P.V.C. diffuses the light giving a standard illumination), or by hanging in front of a standard X-ray viewing-box.

For transport of slides the metal at the top of frame can be withdrawn; the whole plastic framework can then be folded into a neat package and carried in the pocket. The materials to make one such holder cost about 1*s.* 6*d.*

Holders can be made similarly to take $3^1/_4$ in. × $3^1/_4$ in. slides, dental radiographs, or photographic transparencies. For demonstration purposes larger holders can be made to cover the whole of a viewing-box screen.

Sheets of P.V.C. were supplied by Commercial Plastics, and strips ('Vybak') by Bakelite Ltd.

Department of Surgery, University of Durham. J. E. ROGERS.

## BLEEDING ULCER IN A MECKEL'S DIVERTICULUM

SIR,—Complications arise in 11% of cases of Meckel's diverticulum—intestinal obstruction, diverticulitis, and peptic ulceration with hæmorrhage or perforation.

Lecène [1] says that peptic ulcers of Meckel's diverticulum are constantly to be found where the mucosa of the small intestine meets an islet of ectopic gastric mucosa—usually at the base of the diverticulum. This leads to the accepted hypothesis that the peptic activity of this ectopic mucosa produces autodigestion and ulceration of the intestinal mucosa. This concept allows a distinction between ulcers due to inflammation and those due to mechanical causes such as intussusception of the diverticulum.

Intestinal bleeding from these ulcers is usually slight, but sometimes it may be severe, appearing in the stool as red blood and recent clots, and endangering the patient's life.

A boy, aged 2 years, had been in hospital three times in 1955, for whooping-cough, gastrointestinal disorders with generalised urticaria, and an unidentified fever. He had passed some ascarids in the stool. On Nov. 23, 1956, he suddenly became intensely pale, giddy, and cold. His temperature went up to 102·8°F (39·3°C) and next morning he passed a stool almost entirely composed of fresh blood, about 600 ml. At 3 P.M. we noted intense pallor of mucous membranes and skin (pulse 140 a minute, blood-pressure 80/60 mm. Hg). There was periumbilical tenderness, and the abdomen was slightly distended, with transient and local muscular guarding below the umbilicus. No mass could be felt or seen in the rectum, but the exploring finger was stained by fresh blood. An abdominal radiograph showed gas in the intestines without fluid levels. Hæmoglobin 57%, red cells 2·72 million per c.mm., clotting-time 8 min., bleeding-time 3 min.

The presumptive diagnosis was bleeding from an ulcer in a diverticulum, and operation was undertaken on Nov. 24. 300 ml. of whole blood was transfused during the operation and another 300 ml. postoperatively. The small bowel was slightly congested and distended by gas. The large bowel was dark purple and full of blood. About 30 cm. from the ileocæcal junction was a Meckel's diverticulum on the antimesenteric

1. Lecène, cited by Forgue, E. Précis de pathologie externe; vol. II, p. 676. Paris, 1939.

border. Its tip was congested and contained a tumour the size of a lentil. Very many ascarids could be felt in the small intestine. The diverticulum was removed and its stump invaginated without narrowing the lumen of the ileum.

The postoperative course was complicated by persistent paralytic ileus, with abdominal distension and vomiting, which subsided only after continuous gastric suction for 48 hours. An enema returned black blood and clots in great quantity. Intravenous fluids were given. On Nov. 26 the Hb was 72%, and 600 ml. blood was transfused. On the third postoperative day the child was allowed out of bed, and on Dec. 5 he was discharged.

The diverticulum was 4 cm. long, and 1·3 cm. wide at the base. The mucosa was generally of the small-intestine type, but at the tip of the diverticulum was an islet of gastric mucosa. Just near this was an ulcer, smaller than the ectopic tissue, not very deep, covered with a clot of blood. Microscopic examination of the specimen (Dr. H. Breazu, Ploesti) showed at this level a deep layer of tubular glands of gastric type.

The diagnosis was difficult in that the patient had had no previous alimentary-tract hæmorrhages, the illness started with fever, X-ray examination was inconclusive, and there was no umbilical anomaly to point to a diverticulum.

The ulcer is usually situated near the point where the mucosa of the ileum joins that of the diverticulum, but in this case this region was normal. An ulcer at the tip of the diverticulum is very rare, and we have found only one report of such a case.[2]

When one of these ulcers bleeds, operation is always necessary, for death may be caused by continued hæmorrhage into the gut, perforation followed by generalised peritonitis, or ulceration of the mesodiverticulum with intraperitoneal hæmorrhage.[3]

Cimpina Hospital, Rumania.

CONSTANTIN CEPLEANU
ION TUTICA.

## HOOKWORM AND ANÆMIA

SIR,—The association between hookworm infestation and iron-deficiency anæmia is almost traditional. Bilharz first described hookworm in Egypt in 1851. Three years later his pupil Griesinger [4] linked hookworm infestation with the disease called Egyptian chlorosis. Ashford's [5] description (1900) of patients in Puerto Rico with severe anæmia and heavy infestation with the worms received wide recognition. Thereafter ancylostomiasis was regularly added to the list of causes of iron deficiency in standard textbooks of medicine.

Loss of blood at the site of attachment of the worms was generally thought to be the immediate cause of the anæmia. But in recent years some serious doubts have been expressed. The load of worms, as judged by the ova count in the fæces, rarely correlates with the severity of the anæmia. Furthermore patients with an apparently heavy infestation are not always anæmic. The suspicion has grown that the association between hookworm and anæmia is fortuitous, since people infested with the worm commonly live on diets composed chiefly of cereals, poor in proteins, calcium, and ascorbic acid. On such a diet defective absorption of iron would be expected. Foy and Kondi [6]—two hæmatologists with wide experience in the tropics—have summarised present views as follows: "The consensus of opinion then is that hookworms are not a common cause of anæmia, but until more critical work has been done it is better to leave the question open."

2. Moore, C. T. *Surg. Gynec. Obstet.* 1956, **103**, 569.
3. Weese, K. *Zbl Chir.* 1954, **79**, 588.
4. Griesinger, W. *Arch. physiol. Heilkunde*, 1854, **13**, 555.
5. Ashford, B. K. *N.Y. med. J.* 1900, **71**, 552.
6. Foy, H., Kondi, A. *J. trop. Med. (Hyg.)* 1957, **60**, 105.

At this moment of uncertainty we wish to draw attention to the original observations of Boycott and Haldane,[7] who investigated the cause of severe anæmia among tinminers in Cornwall. This had been attributed to bad air, but this explanation they quickly put out of court. Boycott and Haldane found that the men were heavily infested with *Ancylostoma duodenale*, the larvæ of which penetrated their clothing soaked in mine water. Some of the men had less than 40% of hæmoglobin. Such a degree of anæmia in an adult male could not possibly be attributed to any defect in the common British diet of that time.

Boycott and Haldane added a remarkable observation. Using the carbon-monoxide method for measuring blood-volume, developed in Edinburgh by Haldane and Lorrain Smith,[8] they showed that in some of the anæmic Cornish miners the blood-volume was increased, so that the anæmia was due to hæmodilution rather than to loss of blood from the gastrointestinal tract.

We suggest that a properly financed research project into the association between hookworm and anæmia is now overdue.

Departments of Medicine and Physiology, University of Edinburgh.

A. P. MEIKLEJOHN
R. PASSMORE.

## ESSENTIAL FATTY ACIDS, LIPID METABOLISM, AND ATHEROSCLEROSIS

SIR,—In *The Lancet* of April 5 Dr. Keys takes exception to statements contained in our paper which appeared on Feb. 15. If we have misquoted Dr. Keys, we are very sorry indeed. I should, however, like to point out that, in the field of dietary fats, it is very difficult *not* to misquote Dr. Keys, inasmuch as his concepts and statements have differed very radically from one year to the next. Perhaps this is to some degree unavoidable in a field in which knowledge is progressing very rapidly. We should, however, like to suggest that the presentation of precise mathematical formulations that enable one to predict precisely that John Smith's cholesterol level will be precisely so much, in response to precisely so much saturated and unsaturated fat, is very premature indeed. As noted in our paper of Feb. 15, not only the relative but the absolute amount of polyunsaturated fat required to produce a given fall in the level of cholesterol and other plasma-lipids varies markedly with the age of the patient, and the presence of known atherosclerosis. Older individuals with obvious vascular disease may for a time require complete removal of saturated fat from the diet and the administration of large amounts of linoleic-acid-containing fat, in order to obtain a significant and maintained fall in lipids. Young normal individuals may respond to quite modest amounts of polyunsaturated fats in the presence of appreciable amounts of saturated fat.

We can agree in part with Dr. Keys' present thoughts—that is, those of his thoughts stated in his letter in the April 5 issue of *The Lancet*—regarding the relatively "neutral" properties of oleic acid as compared to carbohydrate, if one considers only the effects upon plasma-cholesterol levels. However, the effects upon plasma-triglyceride are very different, inasmuch as, at least in our experience, there is a very marked rise in plasma-triglyceride when carbohydrate is substituted for any type of fat in the diet. This is not observed when highly purified ethyl oleate is administered. Conceivably, the

7. Boycott, A. E., Haldane, J. S. *J. Hyg., Camb.* 1903, **3**, 95.
8. Haldane, J. S., Lorrain Smith, J. *J. Physiol.* 1900, **25**, 33.

elevated triglyceride level with high carbohydrate feeding is in some way related to marked acceleration of lipogenesis.

A final comment concerning "essential-fatty-acid deficiency": an essential nutrient, by definition, is one which cannot be synthesised in the body in adequate amount. If it is not supplied in the diet, its absence will eventually be associated with abnormalities of structure and/or function. Linoleic acid appears to fulfil the requirements of this definition. The fact that, in abnormal individuals, relatively large quantities are required to produce the desired metabolic effects seems to us beside the point, insofar as "essentiality" is concerned. When we have a solid understanding of the way in which linoleic acid lowers plasma-lipid levels, we will be in a much better position to talk of physiologic *versus* pharmacologic effects.

Institute for Metabolic Research,
Highland Alameda County Hospital,
Oakland, California. LAURANCE W. KINSELL.

## ABSENCE FROM WORK ON A MEDICAL CERTIFICATE

SIR,—Dr. Ashworth (April 5) must be given the benefit of the doubt in case he is really trailing his coat. However, he reports the case of the father of two sick children whose wife is working in fear of dismissal, in which it seems indefensible to issue a National Insurance medical certificate.

Humanity should be satisfied, by all means, by giving a note for the respective employer of father or mother stating that their children are ill and require the attention of a parent; but to confuse humanity with "expeditiousness" seems wrong.

To advocate this wide interpretation of sickness certification, whilst expedient, will in fact discredit the National Health Service further (or rather the general practitioner) and substantiate the employers' mistrust of medical certificates. Such interpretation will encourage all the other parents, who as yet are too self-respecting, to follow this example at the next opportunity.

Sickness benefit for a parent is not to be confused with payment for parental duties. The statement which the doctor signs on form Med. 1 is that his patient is incapable of work.

The specious argument—that 5% or 3% of £840 million is a negligible sum, which can be ignored and is cheap at the price for wrongful application of sickness benefits—holds no water. There are many necessary improvements in the Health Service which could be carried out if this sum were available.

Edinburgh. E. V. KUENSSBERG.

SIR,—Many of us will have been given food for thought by Dr. Ashworth's excellent article. One is relieved to see the relative smallness of unjust claims, and this is probably easily offset by those who work when, by all the rules, they should be in bed (though most of us could say from experience that this has surprisingly few ill-effects).

Unless there is clear evidence to the contrary, one has to accept that the patient is giving the facts as he knows them. To start on the assumption that one is being misled, as I suppose a professional referee has to do, would make life impossible; and, anyway, in self-defence one has to play for safety. A patient who collapses with pneumonia or coronary disease after being sent off to work lends no credit to the profession; nor is the man who has to be sent home with a temperature after seeing his doctor on the way to work when his temperature was normal. As Dr. Ashworth says, one may have to observe a patient for a time before making a firm decision.

Arising from this I should like to raise another issue. It seems to me impossible to give an honest note in a large proportion of requests for a day or two's absence. If pressed, one could write a full report in which the pros and cons could be stated, and for which the proper fee would be charged. While giving what is in effect a duplicate of a "panel" note for, say, 2*s*., is a reasonable proposition and a convenience to employer and employee, to certify for 2*s*. that a man is unfit to work today but will be recovered from his lumbago tomorrow is a convenience only to the dishonest. By this means a man can blackmail his employer—who may well know that he was at a football match—into paying him a bonus. This policy has brought certification into contempt both by employer and employee, as I well know from speaking to both: "Anyone", they say, "can get time off if they pay their doctor 2*s*."

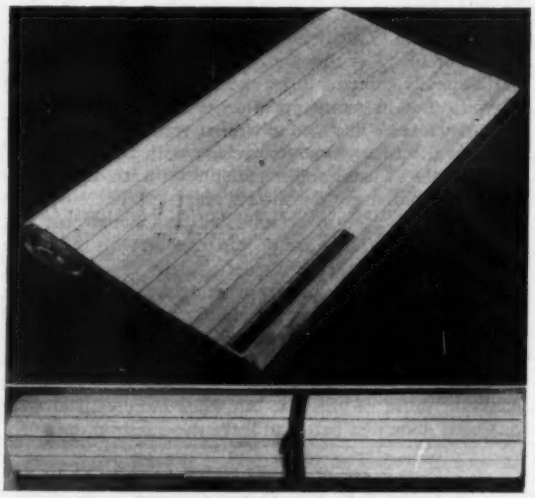
I believe that employers would get less absenteeism if they relied upon a written statement from the worker—the majority of whom are honest—and it would save the genuine patient the inconvenience of waiting in the surgery. It would save the drug-bill the cost of innumerable bottles of medicine which one feels bound to give to relieve symptoms in patients one has decided are not fit for work, and I am sure it would improve the status of doctors if they did not show themselves so ready to be deceived. I know that this has been debated more than once by the B.M.A., but on the grounds I have given I would appeal for a discontinuation of the practice of what is in effect, though not intent, misleading certification.

Shirley, Solihull,
Warwickshire. W. BRIAN GOUGH.

## PORTABLE BED-BOARDS

SIR,—Thousands of people with backache, due to intervertebral-disc and other lesions, now prefer to sleep on hard beds. These people must avoid the well-sprung mattress. Holidays and visits away from home are spoiled by backache through sleeping in comfort.

I have had made for me what might be described as a small tap-mat—made of hard wood and backed with canvas. This can be rolled up, put in a car, and carried round with ease—then laid under a mattress. When rolled



**Above, portable bed-boards; below, rolled for transport.**

it measures only 6 in. in diameter. It has proved a great success.

It was made for me by Messrs. Capes, of Sutton Lane, London W.4. Mr. Cape too has backache, so he took a special interest and now has one for himself.

London, S.W.7. O. S. THOMPSON.

### MODIFIED TRACHEOTOMY TUBE

SIR,—I was most interested to read Dr. Napier's letter of April 5.

Unfortunately he did not illustrate his tube,[1] which he described as "a skeleton tube with open back". It would seem that its main purpose was to facilitate the "weaning" of the child back to normal breathing.

I feel that Dr. Napier has perhaps not fully appreciated the reason for the modifications I describe (March 15). There are in fact several modifications, all equally essential to enable it to perform its function. The tube is designed to facilitate coughing in the acute stages of respiratory infection, such as tracheobronchitis and bronchopneumonia or in chest injuries. It also allows for inflation of the lungs following suction, the use of controlled ventilation should it be required, and the induction of anæsthesia if bronchscopy is necessary.

Alder Hey Children's Hospital, West Derby, Liverpool. FRANK WILSON.

### LONG-TERM ANTICOAGULANT TREATMENT FOR CORONARY ARTERY DISEASE

SIR,—In Dr. Hougie's letter last week I am sure a misprint has occurred. "There is no evidence that there is present in normal plasma a factor which can restore the prolonged bleeding-time of patients with von Willebrand's disease to normal" should surely read "There *is* evidence . . .". Most probably Dr. Hougie is referring to the factor already described by Nilsson et al.[2]

Southern Group Laboratory, Hither Green Hospital, London, S.E.13. P. WOLF.

*** We are grateful to Dr. Wolf for drawing attention to our mistake in reproducing Dr. Hougie's "There is *now* evidence . . ." as "There is *no* evidence . . ."—ED. L.

### PENICILLAMINE AND DIMERCAPROL

SIR,—In his article entitled Penicillamine, a New Oral Therapy for Wilson's Disease, Dr. J. M. Walshe [3] writes:

"A new form of oral treatment with dimethyl cysteine (penicillamine) is described. Given in doses varying from 0·5 to 1·5 gm. daily to six patients with Wilson's disease, it provoked a very large increase in the urine excretion of copper; in five patients it proved more active than BAL in this respect."

Citing Dr. Walshe's article, the statement is often made (e.g., by Dr. Boulding and Mr. Baker [4]), that penicillamine "appears to be more efficacious than dimercaprol".

If two drugs are to be quantitatively compared, equimolar amounts should be given using the same vehicle and the same route of administration; but in Dr. Walshe's studies the penicillamine was given orally by capsule while dimercaprol was administered intramuscularly and probably dissolved in oil.

In a forthcoming article [5] dealing with the ability of penicillamine to protect rats against the lethal effects of mercuric chloride, I present evidence indicating that when equimolar amounts of dimercaprol, *dl*-penicillamine, or *d*-penicillamine dissolved in saline are tested intramuscularly, dimercaprol is definitely superior to *dl*-penicillamine and only slightly superior to *d*-penicillamine under the conditions of our experiments. It would be of interest to compare equimolar amounts of penicillamine and dimercaprol, administered by the same route and in the same vehicle, to determine the relative activities of these drugs on the excretion of copper.

Department of Pharmacology, School of Medicine, Vanderbilt University, Nashville, Tennessee. H. VASKEN APOSHIAN.

1. Napier, W. *Lancet*, 1937, ii, 673.
2. Nilsson, I. M., Blombäcz, M., Jorpes, E., Blombäcz, B., Johansson, S. A. *Acta med. scand.* 1957, **159**, 179.
3. Walshe, J. M. *Amer. J. Med.* 1956, **21**, 487.
4. Boulding, J. E., Baker, R. A. *Lancet*, 1957, ii, 985.
5. Aposhian, H. V. *Science* (in the press).

## Public Health

### More Radioactivity in Britain

Kodak Ltd. make daily measurements of London radioactivity to safeguard their photographic manufacturing processes, and they detected an increase in late March.[1] The activity reached a peak on March 24, when it was 10–20 times normal (it was 100 times the normal after the Windscale accident). The Atomic Energy Authority [2] has since confirmed that there was a "small but sharp" temporary increase in radioactivity over Britain during the second half of March. It is assumed that the increase was due to the recent series of bomb tests in the Soviet Union, and was caused mainly by short-lived fission products. The Authority is to keep a careful watch in the coming months for the longer-lived and more dangerous products.

### Tuberculosis and Cancer in 1957

IN England and Wales last year the death-rate from tuberculosis and the maternal mortality-rate both reached new low records. There were 4250 deaths from respiratory and 534 from other tuberculosis, giving rates per million of 95 and 12 respectively. Since 1947 the death-rate from respiratory tuberculosis has fallen by 79%. The maternal mortality-rate per 1000 live and still births was 0·47 (0·39 excluding abortions). There were 349 deaths from maternal causes (excluding abortion) compared with 399 the year before. These are provisional figures.[3]

The death-rates from cancer were 2312 per million for men and 1891 for women; the figures for 1956 were 2274 and 1891. About 33% of the male and 6% of the female cancer deaths were from lung cancer, and the death-rates from this disease increased from 726 per million in 1956 to 759 for men, and from 111 to 116 for women.

1. *Times*, April 5.
2. *Scotsman*, April 10.
3. Registrar General's Weekly Return for England and Wales, no. 14. H.M. Stationery Office. Pp. 20. 1*s.* 6*d.*

### Infectious Diseases in England and Wales

| Disease | Week ended March | | | | |
|---|---|---|---|---|---|
| | 1 | 8 | 15 | 22 | 29 |
| Diphtheria | 3 | 1 | 1 | 2 | 2 |
| Dysentery | 1333 | 1068 | 1187 | 1173 | 1588 |
| Encephalitis: | | | | | |
| Infective | 3 | 4 | 4 | 4 | 1 |
| Postinfectious | 2 | 1 | 1 | 6 | .. |
| Food-poisoning | 124 | 149 | 144 | 173 | 154 |
| Measles, excluding rubella | 4383 | 4532 | 4012 | 4631 | 4289 |
| Meningococcal infection | 25 | 24 | 29 | 20 | 22 |
| Ophthalmia neonatorum | 40 | 40 | 34 | 37 | 36 |
| Paratyphoid fever | 4 | 6 | 2 | 1 | 4 |
| Pneumonia, primary or influenzal | 773 | 690 | 537 | 514 | 622 |
| Poliomyelitis: | | | | | |
| Paralytic | 10 | 5 | 13 | 21 | 17 |
| Non-paralytic | 5 | 5 | 5 | 6 | 4 |
| Puerperal pyrexia | 226 | 199 | 207 | 205 | 232 |
| Scarlet fever | 797 | 938 | 910 | 965 | 996 |
| Smallpox | .. | .. | .. | 1 | .. |
| Tuberculosis: | | | | | |
| Respiratory | 574 | 591 | 586 | 486 | 545 |
| Meninges and C.N.S. | 11 | 11 | 6 | 9 | 9 |
| Other | 53 | 67 | 68 | 53 | 64 |
| Typhoid fever | 2 | .. | 3 | 2 | 3 |
| Whooping-cough | 525 | 620 | 555 | 587 | 651 |

# Obituary

## JAMES DRUMMOND GRAHAM

Kt., C.B., C.I.E., M.B. Glasg., D.T.M.

Major-General Sir James Graham, formerly public-health commissioner with the Government of India, died on April 4 at the age of 83.

Having been resident physician at the Glasgow Royal Infirmary, he entered the I.M.S. in 1900, and saw military service in Waziristan. Before the first world war, with an appointment in the United Provinces, he was doing valuable work on malaria, showing a decided aptitude for medical research: he was one of a number of senior officers who, under a planned scheme, were making the first malaria survey of all India. For the eight years 1915-23, however, he was away from India—first on the staff of the Egyptian and Mesopotamian expeditionary forces, and later, from 1920, as director-general and inspector-general of the Iraq health services and adviser to the Ministry of Public Health. On his return he became public-health commissioner with the Government of India, and in 1932 he officiated for some months as director-general, I.M.S. In his post as commissioner, writes S. R. C., "he excelled as an administrator. Whilst public-health administration in India was the direct responsibility of Provincial Governments, overruling control of public health and medical research lay with the Central Government, and Sir James Graham played a vital part in development of public health and medical research organisation in India. He was, moreover, no remote and inaccessible official. He worked quietly and understandably in friendly consultation, always helpful and encouraging. He was I think liked by everybody for his friendly simplicity and kindness. There was something very straight and fresh about Graham and one was always stimulated by him. As a Lowland Scot (he came from Ayrshire) he had a streak of canniness in his make-up, but this did not affect his giving ungrudging help and encouragement at all times to the schemes of others."

Internationally he was known to many as delegate for British India in the Office Internationale d'Hygiène Publique, a member for some years of the Health Committee of the League of Nations, and chairman of the advisory committee of the League's eastern health bureau at Singapore. He was appointed C.I.E. in 1919 and C.B. in 1931, and was knighted in 1934, the year of his retirement.

J. M. writes of his "old and greatly valued friend": "His record of services shows that he was selected for a succession of important appointments demanding exceptional qualifications. The many honours conferred on him testify to the conspicuous success with which he filled all these posts. This was due not only to his great professional qualifications but also to his personality, which made him universally popular with his colleagues and others with whom he came into contact, irrespective of race or nationality. It was by no means a case of his being 'hail fellow, well met!' but of his natural friendliness of disposition and his cosmopolitan outlook on life."

He married in 1912 a daughter of Colonel C. Seymour, A.M.S., and they had one son. In later life Sir James and Lady Graham lived for some years in a country house in the south of France. Progressive failure of his eyesight made reading and writing difficult, but did not prevent his corresponding with his friends from Indian days.

# Births, Marriages, and Deaths

## BIRTHS

HADDOCK.—On March 20, in Tanganyika, to May, wife of David Haddock, M.R.C.P.—a son, John Keith.

# Notes and News

## A NATIONAL LIBRARY OF MEDICINE?

A MEMORANDUM prepared by the medical section of the Library Association expresses concern at the decision to omit clinical medicine from the coverage proposed for the National Lending Library for Science and Technology. The need for a national library of medicine, the Association points out, has been felt for many years; for the two largest general medical libraries in this country—those of the Royal Society of Medicine and the British Medical Association—exist to serve their members and have had to reduce the help they used to give other libraries. A national medical library service is needed particularly by the research-worker with non-medical qualifications.

Individual medical schools, postgraduate institutions, and research organisations cannot hope to provide and house libraries sufficiently wide in scope to satisfy from their own resources all the potential needs of their users. Inter-library lending has increasingly become an unsatisfactory answer to the problem of meeting those wide needs.

Moreover the ever-increasing volume of "medical" literature, the increasing variety of forms of publication (to the monograph and journal must now be added the symposium, the research conference proceedings, the project report, the transcript of a tape-recording, and so on), and the diversity of sources from which one form or other of publication comes, demand a correspondingly greater effort for their tracing and acquisition. The individual working library cannot provide that effort. It is better that each should, whilst maintaining a search and acquisition service adequate for its regular needs, be able to turn to a central source.

There appear to be two practicable solutions to the problem of providing a national service of medical literature:

1. A National Library of Medicine could be built on an existing comprehensive medical library.

2. The scope of the new National Lending Library of Science and Technology could be widened to include medicine in its broadest aspects.

The Library Association recommends a thorough examination of the possibility of creating a National Library of Medicine based on the present collections of the Royal Society of Medicine, cooperating and discussing policy with the National Lending Library of Science, as at present envisaged, and making its services available on the same lines. If this proves impossible, the Department of Scientific and Industrial Research should consider covering the whole field of medicine in its broadest aspects by the National Lending Library of Science and Technology.

## TUBERCULOSIS IN THAILAND

IN Thailand, which has some 18 million inhabitants, a tuberculosis service was established by the Thai Government late in 1949, and a central chest clinic—the first of its kind in the country—was set up in the heart of Bangkok. In 1951 the World Health Organisation and UNICEF gave active assistance through the W.H.O. tuberculosis control project, described in our columns by the late Dr. Benatt [1] who became its director. This project was limited to two years, but much of its work has been continued. The central chest clinic has now become the tuberculosis demonstration and training centre, working in association with the tuberculosis hospital at Nonburi, about 15 kilometres from Bangkok. It forms part of the division of tuberculosis control headed by Dr. Prakorb Visalvet, and on the medical side Dr. Nadda Sriyabhaya is the physician in charge.

The average number of deaths attributed to pulmonary tuberculosis in Thailand is about 10,000 a year, giving a mortality-rate of about 60 per 100,000; but the number among

1. Benatt, A. J. *Lancet*, 1956, i, 737.

the 900,000 inhabitants of Bangkok is 1500 (or about 200 per 100,000), and this suggests that outside the capital many cases go unrecognised because facilities for diagnosis are lacking. The percentages of positive reactions obtained (with 5 T.U. of purified protein derivative) in rural areas (5,166,363 persons) and Bangkok (111,727 persons) are:

| *Age-group* | *Rural* | *Bangkok* |
|---|---|---|
| 1–6 | 16·6 | 32·9 |
| 7–14 | 40·4 | 68·1 |
| 15 and over | 78·5 | 88·5 |
| Total | 51·9 | 71·9 |

On mass radiography of some 30,000 people in Bangkok and its neighbourhood during 1953–55 it was found that on miniature film about 5% of the population of Bangkok had an abnormality suggestive of tuberculosis. About 1% were positive on bacteriological examination.

Attendances at the central chest clinic increased from 1500 a month in 1952 to 8000 in 1956. The average number of new patients visiting the clinic is now 800 a month, of whom about 40% are found to have pulmonary tuberculosis. In a month this laboratory handles about 700 direct smears of sputum and about 800 cultures.

Since there is only one tuberculosis hospital, with a capacity of 200 beds, facilities for institutional treatment and isolation are still very limited. As a routine, tuberculosis patients receive two of the three drugs (streptomycin, isoniazid, and P.A.S.), and cases are supervised at home by public-health nurses who give preventive instruction to patient and family. In 1956 a lay visitor was also employed to do home visiting. A refill clinic was also maintained as supplementary treatment, because very few patients were able to take long enough rest.

A contact clinic is held daily to give B.C.G. vaccination to the tuberculin-negative and to examine those with positive X-ray findings. Of 6299 contacts X-rayed during 1953–56, 8% were found to have pulmonary tuberculosis and 1% were positive for tubercle bacilli. As another preventive measure, young children and infants in contact with tuberculosis patients are referred to a central preventorium for children, where they are isolated until B.C.G. has given them a positive tuberculin reaction.

A social service was started last July, and cases referred by the public-health nurses are investigated by the social worker, who reports on their needs. Previously the afflicted families could get some help from the public-welfare department or charitable organisations. During 1956, 102 such families received economic support besides free medical service.

The mass B.C.G. campaign was launched in March, 1953, and 6,652,964 people had been tested, and 2,330,743 negative reactors vaccinated, by the end of 1956. The mass campaign completed, vaccination is entering on a phase of consolidation as part of the permanent national health scheme: that is, the use of vaccine is to be continued on (1) contacts of tuberculosis cases; (2) schoolchildren; and (3) persons at special risk.

The tuberculosis hospital at Nonburi, the only one in Thailand, was incorporated in the tuberculin project in 1951. By the end of 1956 the number of beds had risen from 75 to 200. A thoracic surgical unit was set up in 1952, and major operations in 1952–56 numbered 234. Both the central chest clinic and the hospital have become training centres for student nurses, qualified nurses, medical students, and public-health personnel. To relieve the shortage of nurses a school of nursing aides was started in 1956. The course lasts a year.

## BLOOD-TRANSFUSION

THE Ministry of Health, in association with the Department of Health for Scotland, is shortly issuing a revised edition of *Notes on Transfusion*. This follows closely the lines of the previous one (1954), but certain additions give the text greater clarity. There are also some minor but important alterations: for example, peanut oil has now been omitted from the diet in the treatment of transfusion reaction, and sodium lactate now replaces sodium bicarbonate in the stage of oliguria. Section IX, on the rhesus factor, has been considerably expanded and much improved. Consultants as well as their juniors will find this unassuming little book of 21 pages well worth reading.

## DIAMOND JUBILEE OF R.A.M.C.

IN honour of the diamond jubilee of the Royal Army Medical Corps, a commemorative oration, by Sir Gordon Gordon-Taylor, entitled *In Arduis Fidelis*, will be delivered in the great hall of B.M.A. House, Tavistock Square, London, W.C.1, on Wednesday, June 25, at 5 P.M. The oration will be open to the public without ticket, but past and present members of the Corps, with their ladies, are especially invited.

The British Medical Association played a considerable part in the events that led to the formation of the R.A.M.C. in 1898. For some years it had pressed for reform of the Army's medical organisation, and on Jan. 20, 1898, a deputation from the Association waited upon the Secretary of State for War, Lord Lansdowne, and urged the desirability of forming a single Army Medical Corps. It also expressed the hope "that Her Majesty might be graciously pleased to convert such a corps by Her authority into a Royal Corps, and to give it thereby a position and prestige to which it was fully entitled." [1]

## University of London

The following degrees have been awarded:

*M.D.*—H. B. Hewitt.

*M.S.*—A. J. Davies.

Mr. A. W. Wilkinson, senior lecturer in surgery in the University of Aberdeen, has been appointed to the university chair of pædiatric surgery at the Institute of Child Health.

Mr. Wilkinson qualified M.B. in the University of Edinburgh in 1937, and took the F.R.C.S.E. three years later. In the 1939–45 war he served in the R.A.M.C. in Europe and the Far East, gaining the rank of lieutenant-colonel as officer in charge of a surgical division. Returning to Edinburgh, he held the Syme surgical fellowship from 1946 to 1949, when he was awarded the gold medal for his CH.M. thesis. He was appointed lecturer in surgery at Edinburgh in 1951 and senior lecturer at Aberdeen in 1953. He is at present an assistant surgeon to Aberdeen Royal Infirmary and to the Royal Aberdeen Hospital for Sick Children. His published work includes a book, *Body Fluids in Surgery*, and articles and chapters in books on disturbances of electrolytes and of metabolism in surgical patients.

Dr. A. G. Spencer, first assistant at University College Hospital Medical School and consultant physician to University College Hospital, has been appointed to the university readership in medicine at St. Bartholomew's Hospital Medical College.

## University of Alberta

Dr. T. A. S. Boyd has been appointed associate professor of ophthalmology.

## Hunterian Society

The society's gold-medal essay competition for 1957 has been won by Dr. C. A. H. Watts (Leicester).

The subject for the 1958 essay is Impotence. The competition is open to all general practitioners. Details may be obtained from the hon. secretary, Dr. C. W. Kesson, 51, Harley Street, London, W.1.

## World Congress on Fertility and Sterility

This congress will be held in Amsterdam from June 7 to 13, 1959. Further particulars may be had from the secretary, Dr. L. I. Swaab, Sint Agnietenstraat 4, Amsterdam-C.

## Mental After Care Association

The annual meeting of this association will be held on Wednesday, April 23, at 3 P.M., at the Caxton Hall, London, S.W.1, when General Wilfred Kitching, international leader of the Salvation Army, will give an address.

## Merseyside Medical Art Society

This society was inaugurated at a dinner on April 2, when Sir Philip Manson-Bahr, president of the London Medical Art Society, gave the opening address, to which Lord Cohen of Birkenhead and Prof. Brian Maegraith, the president, replied. The first exhibition, held in the Bluecoat Chambers, included works by doctors in Liverpool, Manchester, Warrington, and Southport. The society's secretary is Dr. D. B. Mossman.

1. *Brit. med. J.* Jan. 29, 1898, p. 330.

### Memorial to Mr. H. R. Segar

Mr. H. Roland Segar became medical superintendent of Barnet General Hospital in 1929 and medical director in 1949. He relinquished this post in 1952 but continued as consulting surgeon till his death. A memorial to him is planned at the hospital, and subscriptions should be sent to Mr. H. D. Cobbe, the treasurer, at 1, Wellhouse Lane, Barnet, Herts.

### Mental Health Research Fund

At the annual meeting on March 25, Lord Monckton, who is chairman of the joint national appeals organisation both of this fund and of the National Association for Mental Health, spoke of the need for the public to support research on mental disorder.

"It would be easy", he said, "to criticise the Government for not devoting a larger proportion of what can be spent on research to medical research; but I have been too lately released from the Government stable to be ready to prefer this sort of criticism without going on to say what research now being undertaken ought to be abandoned to make way for this. . . . Then the criticism has been levelled that, when something between two and three million pounds is being spent by the Medical Research Council, it is wholly wrong to find them spending not more than £56,000 in the field of mental-health research in the year 1957–58; but here again I feel the difficulty (which has not deterred some critics) of pointing out what medical research funds are being spent for purposes that could be abandoned to make way for this." The real answer, he believed, lies in fostering and supporting a voluntary organisation. "A marked and substantial improvement in the response of individual members of the public would be the most effective stimulus to further Government interest." The policy of the Fund had been to encourage more research-workers to enter this field by means of grants and fellowships, and up to last September in three years it had committed itself to spend no less than £50,000. But most of this money had come from generous contributions by the Ford Foundation, and other charitable bodies. "It is, I think, a profoundly disturbing fact that, apart from such contributions, the donations and subscriptions from the British public, including broadcasts and flag-days, to the N.A.M.H. and the M.H.R.F. together, never reached £20,000 in any of the three years 1954–57."

Since last September a further £23,000 has been allocated by the fund to research projects, some being given for expenses and some for fellowships. The recipients are:

Dr. Mildred Creak (psychosis in early childhood); Dr. Ian Cameron (intellectual disintegration in senile dementia); Dr. George Jacobides (puerperal psychoses); Dr. G. Ettlinger (establishment of a Primate Behaviour Research Laboratory); Dr. Denis Parr (alcoholism); Mr. Malcolm Piercy (cerebral localisation of intellectual function); Dr. B. W. Richards (biochemical abnormalities in mental deficiency); Dr. Michael Young (families of mental-hospital patients); Dr. R. T. C. Pratt (biochemical disturbance in endogenous depression); Dr. J. W. B. Douglas and Dr. J. Tizard (behaviour and social ratings of national 1946 sample of children); Dr. T. C. N. Gibbens (clients of prostitutes attending V.D. clinics); Dr. B. R. Gomulicki (perception and learning in blind children); Prof. E. Stengel (suicide); Dr. H. H. Wolff (psychotherapy in bronchial asthma); and Dr. Steven Folkard (follow-up of patients discharged through review and rehabilitation unit).

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Prof. Georg Maurer, chief surgeon of the Munich hospital where members of the Manchester United football team were treated after the recent air crash, has been appointed an honorary C.B.E.

Mr. Arnold Walker has been re-elected chairman and Prof. A. A. Moncrieff deputy chairman of the Central Midwives Board.

Mr. Derek Walker-Smith, the Minister of Health, has appointed Mr. J. T. Woodlock to be his principal private secretary.

A south-western branch of the Dental and Medical Society for the Study of Hypnosis is to be formed and a preliminary meeting for those interested is to be held at the Gloucester Royal Infirmary on Sunday, April 27, at 3 P.M.

A meeting of the Manchester Royal Infirmary Old Residents' Club will be held at the Midland Hotel, Manchester, on Saturday, Oct. 4. All ex-residents will be sent particulars within the next few weeks.

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CORRIGENDUM: *Allergy to Cow's Milk.*—In this annotation (Feb. 8, p. 304) we implied that observations reported by C. Collins-Williams were made in the U.S.A., whereas in fact they were made in Canada.

### Royal Commission on Remuneration

The Royal Commission on Doctors' and Dentists' Remuneration will hold public hearings at 11.15 A.M. on April 24 and 25, at 10, Carlton House Terrace, London, S.W.1. Representatives of the Royal College of Surgeons of England have been invited to attend on Thursday and representatives of the Royal College of Obstetricians and Gynæcologists on Friday.

## Diary of the Week

APRIL 20 TO 26

**Monday, 21st**

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5.15 P.M. Mr. C. P. Wilson: Malignant Disease of the Superior Maxilla.
6.30 P.M. Sir Clement Price Thomas: Carcinoma of the Bronchus.
UNIVERSITY OF LONDON
5.30 P.M. (National Hospital for Nervous Diseases, Queen Square, W.C.1.) Prof. B. D. Burns (McGill): The Problem of Memory.

**Tuesday, 22nd**

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. I. P. Todd: Physiology of Rectal Sensation and its Relationship to Disease. (Arris and Gale lecture.)
6.15 P.M. Mr. Rodney Maingot: Postoperative Strictures of the Bile Ducts.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8 P.M. *Medicine.* Dr. E. R. Cullinan, Dr. Ffrangcon Roberts, Dr. R. R. Bomford: The Physician's Obligation to Society.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. J. Hare: Lymphomata and Reticuloses.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Mr. L. C. Oliver: Contributions of Surgery to the Treatment and Understanding of Parkinsonism.

**Wednesday, 23rd**

ROYAL COLLEGE OF SURGEONS
5.15 P.M. Mr. H. J. Seddon: Surgery of Poliomyelitis.
6.30 P.M. Mr. S. O. Aylett: Ulcerative Colitis.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. O. Oliver: Blood Changes in Skin Diseases.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Mr. O. S. Tubbs: Surgery of Diseases of the Pleural Cavity.

**Thursday, 24th**

ROYAL COLLEGE OF SURGEONS
5.15 P.M. Mr. Wylie McKissock: Surgical Treatment of Intracranial Aneurysms.
6.30 P.M. Prof. C. G. Rob: Arterial Occlusion.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. W. N. Goldsmith: Metabolic Disorders.
MANCHESTER MEDICAL SOCIETY
8 P.M. (Staff House, University of Manchester.) *Anæsthetics.* Dr. M. W. Johnstone: Control of Surgical Shock.

**Friday, 25th**

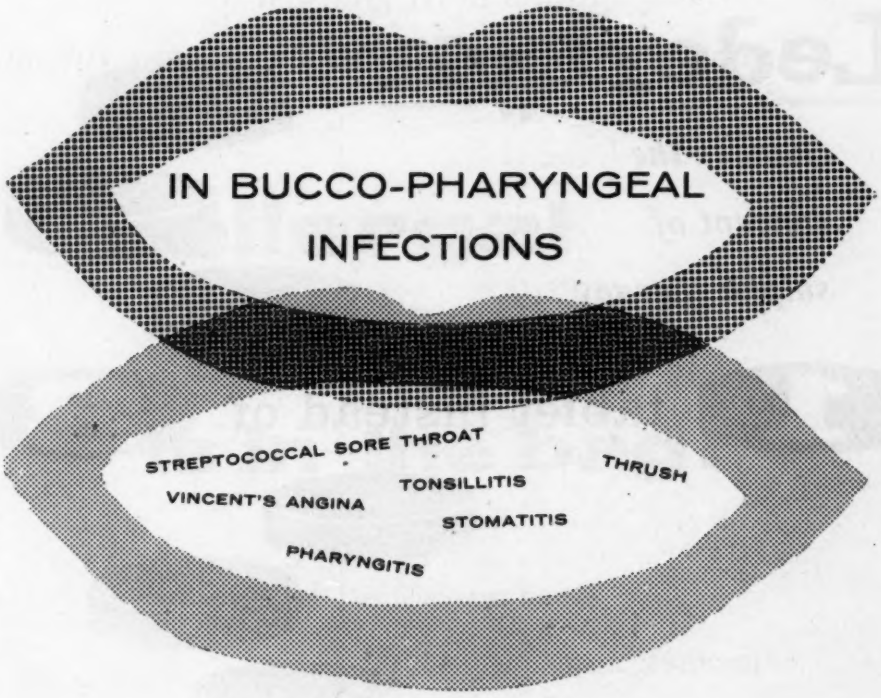
ROYAL COLLEGE OF SURGEONS
5.15 P.M. Mr. N. R. Barrett: Tumours of the Chest Wall.
6.30 P.M. Mr. Victor Riddell: Management of Thyrotoxicosis.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Dr. Imrich Friedmann: Advances in Chemotherapy in Ear, Nose, and Throat Diseases.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. John Peel: Modern Cæsarean Section.

## Appointments

BAINBRIDGE, JEAN M., M.B. Durh., D.OBST.: deputy M.O.H. and deputy principal school M.O., Gateshead.
BROOKS, D. M., M.B. Dubl., F.R.C.S.I.: part-time consultant orthopædic surgeon (with special responsibility for hand surgery), Royal National Orthopædic Hospital, London.
BURNFORD, A. M., M.B.E., M.B. Lond., D.OBST., D.C.H.: assistant M.O., Nottingham.
COTTOM, D. G., M.C., B.M. Oxon., M.R.C.P.: physician, pædiatric department, St. Thomas' Hospital, London.
HIRD, GORDON, M.B. Aberd., D.P.H.: district M.O.H. and port M.O., Boston.
LINN, J. C., M.B. Lond., D.M.R.D.: part-time consultant radiologist, Rotherham group of hospitals.
MCCONNELL, R. B., M.D. Lpool, M.R.C.P.: part-time consultant physician, Broadgreen Hospital, Liverpool.
MANNING, C. W. S. F., F.R.C.S.: part-time consultant orthopædic surgeon and assistant clinical director, Royal National Orthopædic Hospital, London.
PIPER, G. W., M.B. Lond., D.P.H.: deputy M.O.H., Westminster and Holborn, London.
WHITE, JANET M.: M.B. Lond., D.C.H.: assistant M.O., Finchley and Hendon.
ZAUSMER, D. M.: M.B., B.SC., Lond., D.P.M.: consultant in child psychiatry, Birkenhead, Wirral and Chester hospital areas.

**Leeds Regional Hospital Board:**

BIRD, J. D., M.B. Sheff., F.F.A. R.C.S., D.A.: part-time consultant in anæsthetics, East Riding group of hospitals and Hull Royal Infirmary.
SMITH, A. L. G., M.B. Glasg., D.P.M.: consultant in psychiatry, Storthes Hall Hospital, Kirkburton, nr. Huddersfield.
WILKINSON, N. V., M.B. Durh., D.P.M.: assistant psychiatrist (S.H.M.O.), Clifton Hospital, York, and associated clinics.

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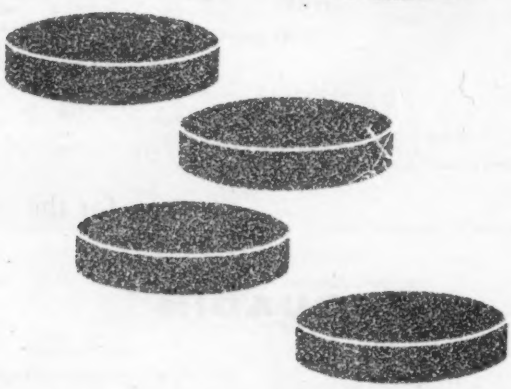

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*Practitioner* (1957) 179, 626

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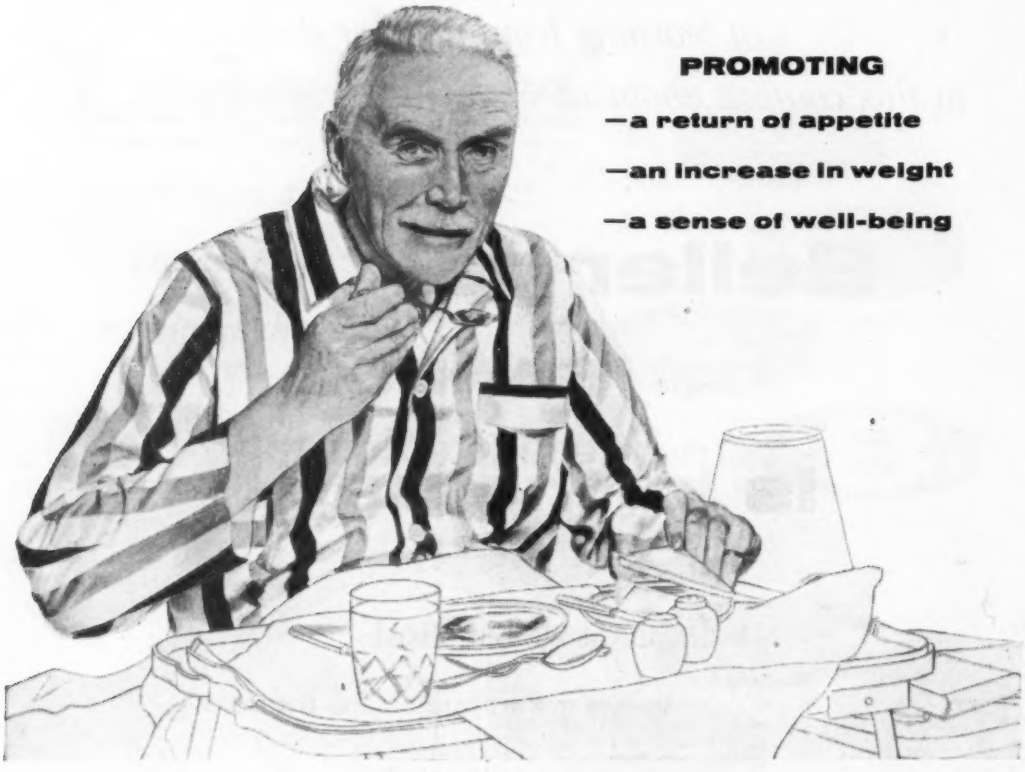

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**—an increase in weight**

**—a sense of well-being**

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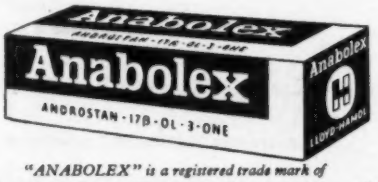
*PRESENTATION: In vials of 25 and 100 tablets, each tablet containing 25 mg. Androstanolone. Anabolex can be prescribed on Form E.C. 10. Basic N.H.S. price 20/- and 70/-.*

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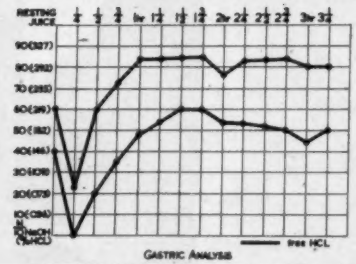
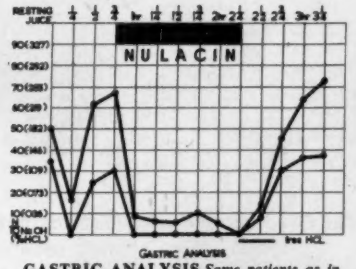



**GASTRIC ANALYSIS** *Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*

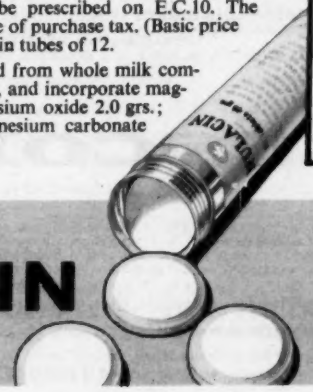



**GASTRIC ANALYSIS** *Same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*

**BIBLIOGRAPHY**


*Practitioner*, 1957, **178:** 43
*Practitioner*, 1956, **176:** 103
*Amer. J. Gastro.* 1956, **26:** 665
*Brit. Med. J.* 1954, **1:** 46


*Further references to the literature and full information on Nulacin available on request.*



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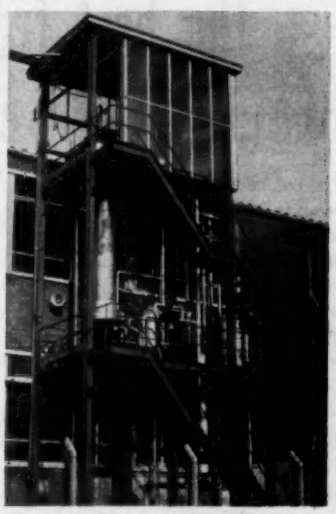

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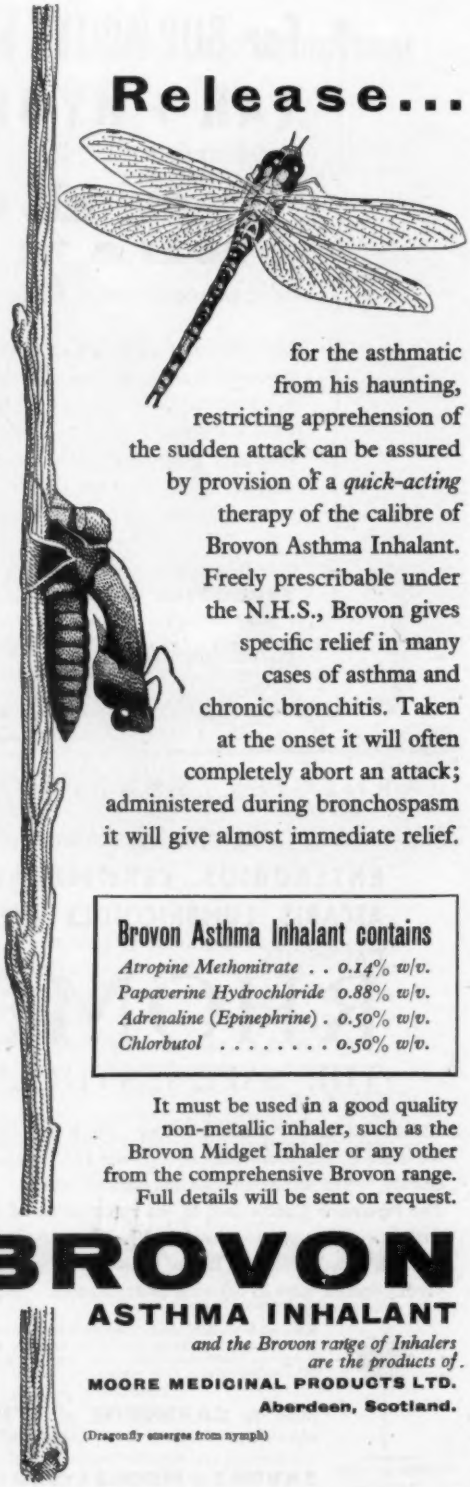

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## Academic and Educational

### FACULTY OF ANÆSTHETISTS OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

ANÆSTHETICS COURSE

A 2 weeks' COURSE OF LECTURES, DEMONSTRATIONS AND TUTORIALS for postgraduates preparing for higher diplomas in anæsthetics will be held from 16TH to 27TH JUNE, 1958.

*Fees:* Lectures and Demonstrations £15 15s.
Tutorial Discussion Groups £10 10s.

Further details and application forms may be obtained from Mr. W. F. DAVIS, Secretary, Faculty of Anæsthetists, Royal College of Surgeons of England, Lincoln's Inn-fields, London, W.C.2 (Tel. HOLborn 3474, ext. 23).

### LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

SCHOLARSHIPS FOR THE 1958–59 DIPLOMA IN PUBLIC HEALTH COURSE

Applications are invited from registered medical practitioners for:—

(*a*) The A. H. BYGOTT SCHOLARSHIP, value £200.
(*b*) 2 ELLISTON MEMORIAL SCHOLARSHIPS, each value £150.
(*c*) The SIR ARTHUR NEWSHOLME MEMORIAL SCHOLARSHIP, value approximately £200.

No tuition fees are charged to successful candidates. Applicants may apply for more than 1 scholarship.

These scholarships are tenable for 1 session at the London School of Hygiene and Tropical Medicine for the course for the University of London's Academic Postgraduate Diploma in Public Health commencing 30th September, 1958.

Applications must be received by 31st May, 1958, by the Dean, London School of Hygiene and Tropical Medicine, Keppel-street, (Gower-street), London, W.C.1, from whom application forms may be obtained.

### THE WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY

ST. MARY'S HOSPITAL MEDICAL SCHOOL, London, W.2

The FIRST ALMROTH WRIGHT LECTURE will be given by Professor C. L. OAKLEY, M.D., F.R.S., University of Leeds, in the lecture-theatre of the above Institute on MONDAY, 28TH APRIL. Subject: "Sites of Production of Antibodies".

The lecture is open to all members of the medical profession and to all students in medical schools without fee.

### UNIVERSITY COLLEGE LONDON

FREE PUBLIC LECTURES, SUMMER TERM 1958

FRIDAY and TUESDAY, 25TH, 29TH APRIL, at 5.30 P.M. Dr. B. DELISLE BURNS, (1) Networks of Self-reexciting Neurones; (2) The Responses of Neurones in the Cerebral Cortex to Polarisation.

MONDAY, 5TH, 12TH MAY, at 5 P.M., Dr. B. A. STONE, The Biochemistry of Cellulose and Related Polysaccharides.

Complete list of public lectures from Publications Officer, University College London, Gower-street, W.C.1 (stamped envelope required).

### GLASGOW ROYAL INFIRMARY

DR. JOHN MACINTYRE MEMORIAL LECTURE

Professor B. W. WINDEYER, of the Meyerstein Institute of Radiotherapy, The Middlesex Hospital, London, will deliver the above Lecture entitled "John Macintyre: A Prophecy in Retrospect", in the Lister Lecture Theatre, Glasgow Royal Infirmary, on WEDNESDAY, 30TH APRIL, 1958, at 5 P.M.

### THE UNIVERSITY OF MANCHESTER

DIPLOMA IN AUDIOLOGY

The Department of Education of the Deaf with the cooperation of the Department of Otolaryngology will hold, in 1958–59, a 1-year course leading to a Diploma in Audiology. This advanced course will be open to registered medical practitioners, including medical officers, also to qualified teachers of the deaf, qualified psychologists and speech therapists.

The course will include the causation of deafness, physical audiology, including the application of experimental phonetics, measurement of hearing, psychology of deafness, and the educational treatment of deafness. The course will open on 2ND OCTOBER, 1958.

Forms of application and further information may be obtained from the Director of the Department of Education of the Deaf, the University, Manchester, 13.

### THE UNIVERSITY OF SHEFFIELD

COURSES OF INSTRUCTION for the Diplomas (of the English Conjoint Board) in Medical Diagnostic Radiology (D.M.R.D.) and Therapeutic Radiology (D.M.R.T.) will commence in OCTOBER, 1958. The courses will cover a period of 2 years of whole-time study, and the fee for each course is £60.

Applications to attend should be sent to the Dean of the Faculty of Medicine, The University, Sheffield, 10.

**UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.** A vacancy exists for a QUALIFIED TECHNICIAN for Poliomyelitis Research under Professor WILSON SMITH, F.R.S. Suitable B.SC. graduate might be considered.

Terms and salary scale on application to the Secretary, University College Hospital Medical School, University-street, London, W.C.1.

**UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.** A vacancy exists for an ASSISTANT in the Department of Bacteriology under Professor WILSON SMITH, F.R.S. Medical qualification preferred. Previous laboratory experience an advantage. Duties include some teaching and poliomyelitis research. Commencing salary range £960–£1100 p.a. plus superannuation.

Applications within 10 days to the Secretary, University College Hospital Medical School, University-street, London, W.C.1.

**UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.** A vacancy exists for a BIOCHEMIST experienced in techniques for steroid estimation, for research appointment with clinical endocrinology.

Apply in writing to the Secretary, University College Hospital Medical School, University-street, London, W.C.1.

**FACULTY OF ANÆSTHETISTS OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND.** Applications are invited from qualified medical practitioners of British nationality, specialising in anæsthetics, for a BURROUGHS WELLCOME FELLOWSHIP in Anæsthesia tenable at the University of California Medical Center, Los Angeles, for a period of 1 year, value $4000.

Further information may be obtained from Mr. W. F. DAVIS, Secretary, Faculty of Anæsthetists, Royal College of Surgeons, Lincoln's Inn-fields, London, W.C.2.

**INSTITUTE OF OPHTHALMOLOGY (University of LONDON), Judd-street, W.C.1.** Applications are invited for the SHEPHERD RESEARCH FELLOWSHIP, tenable for 3–5 years in the Department of Pathology, to be devoted to the immunological problems of ocular disease. Previous experience in this field desirable but not essential; applicants need not be medically qualified.

Applications by 1st May, 1958, with names of 2 referees, to Director, Department of Pathology, at above address, from whom further particulars may be obtained.

**UNIVERSITY OF BRISTOL.** Applications are invited for appointments as DEMONSTRATOR IN PATHOLOGY. Salary scale at present £900–£50–£1100 p.a. according to qualifications and experience. Previous experience in pathology is not necessary. The duties include assistance with the teaching of medical and dental students and general pathology for veterinary students, and the conduct of autopsies. Facilities for research and experience of diagnostic histology are available.

Applications, giving full name, age, qualifications, details of education and experience, together with the names of not more than 3 referees, should reach the undersigned, from whom further particulars may be obtained, on or before 25th April, 1958.

H. C. BUTTERFIELD, Registrar and Secretary.

**UNIVERSITY OF EDINBURGH. Department of Ophthalmology.** Applications are invited for the post of LECTURER in the Department of Ophthalmology. Salary scale £1400–£100–£1900 p.a., with placement according to qualifications and experience, and with superannuation benefit and family allowance where applicable. Although the holder of the appointment will be required to devote a large part of his time to teaching and research, there will also be opportunities for both clinical and operative work. The successful applicant will be required to take up duty on 1st October, 1958.

Further particulars may be obtained from the undersigned, with whom applications, giving the names of 3 referees, should be lodged not later than 15th May, 1958.

CHARLES H. STEWART, Secretary to the University.

April, 1958.

**UNIVERSITY OF SOUTHAMPTON.** Applications are invited for the post of LECTURER or ASSISTANT LECTURER IN BIOCHEMISTRY in the Department of Comparative Physiology and Biochemistry. Higher degree in biochemistry, physiology or pharmacology necessary. Salary scale: Lecturer, £900–£50–£1350–£75–£1650; Assistant Lecturer, £700–£50–£850, with placing according to qualifications and experience. F.S.S.U. and children's allowances.

Further particulars should be obtained from the Secretary and Registrar, to whom applications (7 copies from United Kingdom applicants) should be sent not later than 10th May, 1958.

**UNIVERSITY OF ST. ANDREWS. Queen's College, DUNDEE.** Applications are invited for the post of LECTURER IN OPERATIVE DENTAL SURGERY, Dental School, Queen's College, University of St. Andrews. Salary scale £900–£100–£1900 (efficiency bar £1400); placing according to qualifications; F.S.S.U.; family allowance; honorary appointment from Eastern Regional Board as Clinical Assistant in Dundee Dental Hospital attached to post.

Applications (7 copies), with names of 3 referees, to the undernoted, not later than 10th May, 1958.

PATRICK CUMMING,
Joint Clerk to the University Court,
Queen's College, Dundee.

April, 1958.

**THE UNIVERSITY OF ALBERTA, Canada.** Applications are invited from medical graduates for the combined post of ASSOCIATE PROFESSOR OF BACTERIOLOGY (equivalent to Senior Lecturer) AND SENIOR ASSISTANT BACTERIOLOGIST, Provincial Laboratory and University Hospital. Candidates should have experience of teaching and of medical diagnostic bacteriology. Initial salary $10,000; tax free removal grant. A more junior appointment may also be considered.

Applications and enquiries should be sent to the Dean, Faculty of Medicine, University, Edmonton, Alberta, Canada.

**THE UNIVERSITY OF MANITOBA.** Applications are invited for the CHAIR OF BIOCHEMISTRY in the Faculty of Medicine. Minimum qualifications: M.D. with special training in Biochemistry, or Ph.D. in Biochemistry. Teaching and research experience essential. Salary in the range of $10,000, depending on qualifications and experience.

Address applications or enquiries to L. G. BELL, M.D., Dean, Faculty of Medicine, The University of Manitoba, Emily and Bannatyne, Winnipeg 3, Manitoba, Canada.

**WESTERN RESERVE UNIVERSITY SCHOOL OF MEDICINE, CLEVELAND, OHIO, U.S.A.** A FELLOWSHIP IN PEDIATRIC RENAL RESEARCH will be available beginning 1st July, 1958, in the Department of Pediatrics, at above University School. The candidate would be expected to spend approximately two-thirds of his time in laboratory research and one-third in clinical work with patients under investigation. Salary will be $4500–$5000. Applicants with minimum training of 2 years in pediatrics preferred.

Direct correspondence to WALTER HEYMANN, M.D., 2103, Adelbert-road, Cleveland 6, Ohio, U.S.A.

## Hospital Services: Senior Appointments

**NATIONAL HOSPITALS FOR NERVOUS DISEASES.** The Board of Governors invites applications for the Whole-time appointment of ASSISTANT CLINICAL PATHOLOGIST, paid in the salary scale of a Senior Hospital Medical Officer, at The National Hospital, Queen-square, London, W.C.1. Candidates should hold higher qualification.

Applications (36 copies), giving the names of 3 referees, must be submitted to the undersigned not later than 10th May, 1958.

H. EWART MITCHELL, Secretary to the Board of Governors.
Queen-square, W.C.1.

**ST. MARK'S HOSPITAL FOR DISEASES OF THE** RECTUM AND COLON, City-road, London, E.C.1. CLINICAL ASSISTANT (honorary) required in Outpatient Clinic on Thursday afternoons.

Further particulars obtainable from Secretary.

**ST. THOMAS'S HOSPITAL, London, S.E.1. Assistant** RADIOLOGIST to the X-ray Diagnostic Department. Whole-time. Salary £1653 15s.–£2126 5s. p.a.

Applications, naming 2 referees, to the Clerk of the Governors by 30th April, 1958.

**BIRMINGHAM REGIONAL HOSPITAL BOARD.**

(*a*) Part-time CONSULTANT SURGEON (7 notional half-days weekly). Duties at Guest Hospital, Dudley (3 notional half-days) and Corbett Hospital, Stourbridge (4 notional half-days). Higher qualification and wide experience specialty essential.

(*b*) Whole-time CONSULTANT PSYCHIATRIST AND DEPUTY MEDICAL SUPERINTENDENT. Duties at Lea Colony, Bromsgrove (342 Beds), and Lea Castle Colony, Kidderminster (160 Beds). D.P.M. and wide experience specialty essential. Accommodation available at Lea Colony.

(*c*) Whole-time SENIOR CASUALTY OFFICER required at Burton-on-Trent General Hospital. Salary within scale £1653–£2126 p.a. Tenable up to 4 years. Higher qualification an advantage.

Applications (15 copies), stating age, nationality, qualifications, present and previous appointments, and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 19th May, 1958.

**BIRMINGHAM REGIONAL HOSPITAL BOARD.** Applications are invited from duly qualified medical practitioners for the whole-time post of DEPUTY SENIOR ADMINISTRATIVE MEDICAL OFFICER at a salary of £1995–£105 (5)–£2520 p.a., subject to National Health Service (superannuation) regulations. Experience in hospital administration essential; D.P.H. an advantage. Duties: to assist the Senior Administrative Medical Officer in the planning, organisation, and staffing of the hospital and specialist services of the region, and such administrative and executive functions as may be assigned to him.

Applications (15 copies), stating qualifications and experience, together with the names of 3 referees, should be addressed to the Secretary of the Board (from whom further particulars of the post may be obtained) at 10, Augustus-road, Edgbaston, Birmingham, 15, by 3rd May, 1958. Canvassing will disqualify.

**BRISTOL CLINICAL AREA. South Western Regional** HOSPITAL BOARD. Applications are invited for the appointment of a CONSULTANT PHYSICIAN with an interest in neurology in the Bristol Clinical Area. The appointment will be held on a maximum part-time (9 sessions) basis. The successful candidate, who will have charge of beds at Southmead Hospital and at Cossham or Frenchay Hospitals, will undertake regular sessions at Snowdon Road Hospital: he will also be required to visit other hospitals in the clinical area as determined by the Regional Board.

Applications (14 copies), stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 10th May, 1958.

**EXETER CLINICAL AREA. South Western Regional** HOSPITAL BOARD. Applications are invited for the appointment of a DENTAL SURGEON in the Exeter Clinical Area. The appointment will be on a part-time basis (1 session weekly) in the Senior Hospital Dental Officer grade. The successful candidate will be appointed to work mainly at Newton Abbot Hospital but may be required to undertake duties in other hospitals in the clinical area as determined by the Regional Board from time to time.

Applications, stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 5th May, 1958.

**LINGFIELD HOSPITAL SCHOOL FOR EPILEPTIC** CHILDREN. Applications are invited for the post of DEPUTY MEDICAL SUPERINTENDENT to commence duties in the Autumn. Neurological or pædiatric experience desirable. Mainly medical but some administrative duties. Salary according to the scale for Senior Hospital Medical Officers. A house is available at a nominal rent for a married man. Superannuable under F.S.S.N.

Applications, stating age, marital status, full particulars of qualifications and experience and names of 2 referees, to be sent to the Medical Superintendent, Lingfield Hospital School, Lingfield, Surrey.

**LIVERPOOL REGIONAL HOSPITAL BOARD. Birken-** HEAD GROUP. Applications are invited for the post of Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer) in the above Group with duties mainly at St. Catherine's Hospital. Applicants should have general all-round experience in clinical pathology. The possession of a higher qualification in pathology will be considered an advantage.

Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be returned not later than 3rd May, 1958.

VINCENT COLLINGE, Secretary to the Board.

**LEEDS REGIONAL HOSPITAL BOARD.**

CONSULTANT in Pathology, Hull A and B Groups (whole-time or maximum part-time). The person appointed will be responsible for the bulk of the hæmatological and serological work in the Groups and will be based at the Kingston General Hospital. Residence in the Hull area essential.

CONSULTANT in General Surgery (8 notional half-days per week), Scarborough, Bridlington, Malton and Whitby Group. Duties mainly at Scarborough Hospital (20 hours per week). 1 session weekly at Whitby War Memorial Hospital. Residence in Scarborough area essential.

CONSULTANT in Orthopædic Surgery (maximum part-time), Scarborough, Bridlington, Malton and Whitby Group. Duties mainly at Scarborough Hospital (12 hours per week). 1 session weekly at Lloyd Hospital, Bridlington. Fortnightly sessions at Malton and Whitby. 9 hours per week to be devoted to Adela Shaw Orthopædic Hospital and associated clinics in the North Riding area. Residence in Scarborough area essential.

Applications (12 copies), stating age, qualifications and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 20th May, 1958.

**LEEDS REGIONAL HOSPITAL BOARD. Consultant** in Child Psychiatry (whole-time or maximum part-time). Duties at Child Psychiatric Clinics of the County Boroughs of Wakefield and Dewsbury (2 sessions per week each); remainder (5 or 7 sessions) at West Riding County Council Clinics at Wakefield, Mirfield, Shipley, Skipton, Goole, and Todmorden. The Board will also consider applications from suitably qualified practitioners for limited sessions only. Candidates should indicate how many sessions they can undertake and at which centre or centres.

Applications (12 copies), stating age, qualifications and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 20th May, 1958.

**GUILDFORD. ROYAL SURREY COUNTY HOSPITAL.** LOCUM TENENS required for Consultant Orthopædic Surgeon for 9 sessions per week from 1st to 31st May. Includes Accident Department.

Applications, stating qualifications, age and experience, to the Hospital Secretary as soon as possible.

**MANCHESTER REGIONAL HOSPITAL BOARD. Whole-** time NON-RESIDENT SENIOR CASUALTY OFFICER at Salford Royal Hospital, near Manchester. Appointee will work under general supervision of consultants. Tenure of post limited to 4 years; salary within range £1653 15s.–£52 10s.–£2126 5s. p.a. (according to experience, &c.).

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by 29th April, 1958.

**MANCHESTER. UNITED MANCHESTER HOSPITALS** AND MANCHESTER REGIONAL HOSPITAL BOARD. CONSULTANT CARDIOLOGIST (9 sessions). Duties will include the development and supervision of a Pædiatric Cardiac Diagnostic Unit at St. Mary's Hospital, in collaboration with the University Department of Child Health (3 sessions); consultant duties in the University Department of Cardiology, Manchester Royal Infirmary (4 sessions); and in Regional Board Hospitals in Manchester (2 sessions). Candidates must possess a higher qualification in medicine.

Applications (12 copies) should be sent to the undersigned not later than 17th May, 1958, with the names of 3 referees.

F. J. CABLE, Secretary to the Board of Governors.
United Manchester Hospitals, Oxford-road, Manchester, 13.

**NORTH EAST METROPOLITAN REGIONAL HOS-** PITAL BOARD.

**Tilbury and S.E. Essex Group of Hospitals**

Part-time CONSULTANT E.N.T. SURGEON for 3 sessions a week. Duties at Tilbury and Riverside Hospital, and St. Andrew's Hospital, Billericay.

**Ilford Child Guidance Clinic**

Part-time CONSULTANT PSYCHIATRIST for 2 sessions a week.

**Hertford Group of Hospitals**

Part-time CONSULTANT RADIOLOGIST for 3 sessions a week. Duties at Herts and Essex General Hospital, Bishop's Stortford (2 sessions) and County Hospital, Hertford (1 session).

Applications (6 copies), stating post concerned, and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 17th May, 1958.

**NORTH WEST METROPOLITAN REGIONAL HOS-** PITAL BOARD.

1. CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST, whole-time or maximum sessions, Luton and Hitchin Group of hospitals (total beds approximately 120 for obstetrics and 51 for gynæcology). The duties will be mainly obstetrical at present and the general direction of the departments will remain with the existing Consultants. Hospitals may be visited by arrangement with the Group Secretary at St. Mary's Hospital, Luton.

Applications before 19th May, 1958.

2. CONSULTANT SURGEON, 2 half-days a week, Finchley Memorial Hospital, Granville-road, North Finchley, N.12 (76 Beds). Post vacant 30th September, 1958.

Applications before 27th May, 1958.

3. CONSULTANT E.N.T. SURGEON, 2 half-days a week, Mount Vernon Hospital, Northwood (551 Beds). The Hospital is a regional centre for radiotherapy and special experience of malignant diseases of the ear, nose and throat is desirable.

Applications before 29th May, 1958.

4. CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST, 2 half-days a week, Royal London Homœopathic Hospital, Great Ormond-street, W.C.1 (183 Beds).

Applications before 30th May, 1958.

Hospitals may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

**NEWCASTLE REGIONAL HOSPITAL BOARD.** Consultant ANÆSTHETIST, whole-time or maximum part-time, for Newcastle upon Tyne Group of hospitals (total bed complement 1700 Beds); main hospital Newcastle General (835 Beds).

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

**NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS AND NEWCASTLE REGIONAL HOSPITAL BOARD.** Applications are invited for the post of ASSISTANT SURGEON at the Royal Victoria Infirmary under the Board of Governors and SURGEON with the Regional Hospital Board. The appointment will be of Consultant status and will be on a maximum part-time basis, with 5 sessions at the Teaching Hospital under the Board of Governors and 4 sessions in hospitals under the control of the Gateshead Hospital Management Committee under the Newcastle Regional Hospital Board.

Applications, giving full details and names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

**OXFORD REGIONAL HOSPITAL BOARD.** Assistant PSYCHIATRIST (Senior Hospital Medical Officer grade), whole-time to the Fair Mile Hospital, near Wallingford, Berkshire, and its associated clinics, as a member of the area team. Residential accommodation is available. Candidates should hold the D.P.M. or its equivalent and must have had considerable experience of psychiatry. Applicants are invited to visit the hospitals by arrangement with the Physician-Superintendent.

Applications (10 copies), stating age, qualifications, and experience, with the names of 3 referees, should reach the Secretary, Oxford Regional Hospital Board (from whom further particulars are available), 43, Banbury-road, Oxford, by 10th May.

**ROCHESTER. ST. BARTHOLOMEW'S HOSPITAL.** Locum ORTHOPÆDIC CONSULTANT required. 2 sessions weekly during period 8th May–5th July, 1958.

Applications, giving full details, to Group Secretary, Medway and Gravesend Hospital Management Committee, 20, Star-hill, Rochester Kent.

**SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD.** Applications are invited for a Whole-time post of SENIOR HOSPITAL MEDICAL OFFICER in Anæsthetics at the Stornoway Hospitals. Duties are mainly at the Lewis Hospital, where a rented house is available for the officer.

Schedules of application and further particulars are obtainable from the undersigned, with whom applications should be lodged by 9th May, 1958.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Reay House, 17, Old Edinburgh-road, Inverness.

**SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the appointment of Whole-time ASSISTANT RADIOTHERAPIST at the Western Infirmary, Glasgow. Salary (at age 32 and over) on the scale £1653 15s.–£52 10s.–£2126 5s.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

**SOUTH RUISLIP, MIDDLESEX. THE UNITED STATES AIR FORCE HOSPITAL, SOUTH RUISLIP, MIDDLESEX,** has a vacancy on the medical staff for a qualified PÆDIATRICIAN.

Interested Medical Officers should write to the Hospital Commander, U.S. Air Base, South Ruislip.

**SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** requires Whole-time Locum ASSISTANT PHYSICIAN (Senior Hospital Medical Officer grade) for the Wandle Valley Hospital, Mitcham Junction, Surrey. The Hospital is for fever and chronic sick cases, and candidates should have experience in fevers. The post will be tenable for 6 months (commencing July, 1958) in the first instance, subject to renewal. Remuneration £34 14s. 6d. per week.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 10th May, 1958. Applicants may visit Hospital by local arrangements.

**SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** requires Whole-time ASSISTANT GERIATRIC PHYSICIAN (Senior Hospital Medical Officer grade) for duties in the part of Surrey incorporating the areas served by the Farnham and the Woking and Chertsey Groups of hospitals. The appointment will be a joint one between the Board and the Surrey County Council. Candidates should have a good general medical experience and genuine interest in the welfare and treatment of the elderly and infirm. The duties attached to the appointment will include responsibility for determining the type of accommodation or service of which particular patients are in need.

Application by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 10th May, 1958. Applicants may visit the Groups concerned by local arrangement.

**WELSH REGIONAL HOSPITAL BOARD.** Consultant RADIOLOGIST, Merthyr and Aberdare Hospital Management Committee. Based at Merthyr General Hospital with visits to other hospitals in the group. Successful candidate will be required to live within the area. Optional whole-time/maximum part-time appointment.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

**WELSH REGIONAL HOSPITAL BOARD.** Whole-time Locum Tenens CONSULTANT ORTHOPÆDIC AND TRAUMATIC SURGEON required Clwyd and Deeside Hospital Management Committee area immediately.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

**WELSH REGIONAL HOSPITAL BOARD.** Whole-time Locum Tenens CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST required West Wales Hospital Management Committee area 14th September–12th October, 1958.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

**WELSH REGIONAL HOSPITAL BOARD.** Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer), Whitchurch Hospital, near Cardiff. Hospital provides all modern methods of treatment and accommodates approximately 871 patients (Male and Female). Candidates should hold the D.P.M. and have had a wide experience in psychiatry. The successful applicant will work under the direction of the Consulting Psychiatrists.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

**WELSH REGIONAL HOSPITAL BOARD.** Whole-time Locum Tenens CONSULTANT RADIOLOGIST required, Newport and East Monmouthshire Hospital Management Committee and North Monmouthshire Hospital Management Committee, immediately.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

**DUBLIN. NATIONAL CHILDREN'S HOSPITAL, AND UNIVERSITY OF DUBLIN (TRINITY COLLEGE).** Applications are invited for the whole-time joint appointment of CLINICAL PATHOLOGIST AND PATHOLOGICAL TUTOR, to work in the Hospital and in the Medical School of the College. The combined emoluments attached to the joint appointment will be not less than £2000 p.a.

Further information may be obtained from the Registrar, Trinity College, Dublin, who will receive applications until 17th May, 1958.

**DUBLIN. ROYAL CITY OF DUBLIN HOSPITAL, AND UNIVERSITY OF DUBLIN (TRINITY COLLEGE).** Applications are invited for the whole-time joint appointment of CLINICAL PATHOLOGIST AND TUTOR IN PATHOLOGY, to work in the Hospital and in the Medical School of the College. The combined emoluments attached to the joint appointment will be in the range £1300–£2100 p.a.

Further information may be obtained from the Registrar, Trinity College, Dublin, who will receive applications until 17th May, 1958.

**ADDIS ABABA, ETHIOPIA. PRINCESS TSAHAI MEMORIAL HOSPITAL.** SENIOR SURGEON; salary E$24,000 a year less tax. 3-year contract; 1 month annual leave (cumulative). Flat, furniture, car, and petrol supplied.

Application form and further details from Honorary Secretary, Princess Tsahai Memorial Hospital Council, 2, Ross-court, Putney Hill, S.W.15.

**ADDIS ABABA, ETHIOPIA. PRINCESS TSAHAI MEMORIAL HOSPITAL.** SENIOR GYNÆCOLOGIST, to start midwifery school. Salary E$1800 a month less tax. 3-year contract; 1 month annual leave (cumulative). Flat, furniture, car, and petrol supplied.

Application form and further details from Hon. Secretary, Princess Tsahai Memorial Hospital Council, 2, Ross-court, Putney Hill, S.W.15.

**MELBOURNE. ST. VINCENT'S HOSPITAL. University OF MELBOURNE.** Applications are invited for the position of DIRECTOR of the Clinical Biochemical Laboratories of St. Vincent's Hospital, Melbourne.

Qualifications: Medical graduate with extensive training in clinical biochemistry and expert knowledge of biochemical investigation in the problems of general medicine.

Salary: £3000 Australian with increments of £100 to £3500 Australian. Limited private practice within the Department may be allowed.

Superannuation is available. Reasonable travelling expenses will be allowed for successful applicant.

Applicants should furnish details of their nationality, age, marital status, experience and published work. 2 testimonials should be submitted and the names of 3 referees who may be consulted.

Further information may be obtained from the Chief Executive Officer and Secretary, St. Vincent's Hospital, Victoria Parade, Melbourne, N.6, Victoria, Australia.

E. W. R. GRACE, Chief Executive Officer and Secretary.

**NEW ZEALAND. THE OTAGO HOSPITAL BOARD. DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY, DUNEDIN HOSPITAL, NEW ZEALAND.** Applications are invited for the position of SENIOR VISITING OBSTETRICIAN AND GYNÆCOLOGIST, Dunedin Hospital, New Zealand. Applicants must hold a higher qualification in obstetrics and gynæcology with corresponding postgraduate experience. The salary payable in accordance with the Hospital Employment (Medical Officers) Regulations is £775 p.a., and subject to appointment by the University of Otago there will be a further remuneration as a Tutor in Obstetrics. The hours of duty of the appointee will be from 7 to 10½ hours per week, and private practice will be permitted. Conditions of appointment for the position may be obtained from THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2, or the office of the High Commissioner for New Zealand, 415, The Strand, London.

Applications, on the application form attached to the conditions of appointment, stating age, qualifications and experience, together with copies of recent testimonials and health and radiological certificates, will be received by the undersigned until 10 o'clock A.M. on Monday, 2nd June, 1958.

W. A. WILLIAMSON, Secretary, Otago Hospital Board.
P.O. Box 946, Dunedin, New Zealand.

**SINGAPORE. ROYAL SINGAPORE TUBERCULOSIS** CLINIC. Singapore Anti-Tuberculosis Association. Applications are invited for the appointment of a CHEST PHYSICIAN. The appointment is for 3 years with the option of further periods of 3 years. The commencing salary is S.$1200 per month, rising to S.$1600 per month, with further S.$100 per month cost-of-living allowance. Annual increments are by S.$50 per month annually. (Sterling equivalent £1675 p.a., rising to £2230 p.a. Cost-of-living allowance £140 p.a. Increments £70 p.a.) Passages will be paid both ways for a 3-year agreement and 1 month's full-pay leave will be granted for each year of service. There is also a provident fund, to which the officer subscribes 5 % and the Association 10 % of the salary. Contributions to this are realisable on both counts after 5 years' service. After less than 5 years' service those paid by the employee are refunded, plus interest accrued. Applicants should have a higher qualification and not less than 1 year's exclusive experience of tuberculosis of the chest. Special experience might entitle the applicant to a higher starting salary than that mentioned above.

Further information can be obtained from the Secretary, NAPT, Tavistock-square, London, W.C.1, or from the Medical Director, SATA, Singapore, 2.

## Hospital Services: Junior Appointments

**ALBERT DOCK ORTHOPÆDIC AND FRACTURE** HOSPITAL, Alnwick-road, E.16. SEAMEN'S HOSPITALS GROUP. SENIOR HOUSE OFFICER (surgery) required on 17th May, 1958. Post, which is normally resident, is recognised by the Royal College of Surgeons, and provides excellent experience in a wide variety of traumatic conditions received from the adjacent dockland and from shipping in the Port of London. Salary £819 10s.

Applications, stating age, nationality, qualifications, and experience, with the names of 2 recent referees, should be sent to the Secretary, Dreadnought Seamen's Hospital, Greenwich, not later than 1st May.

**BATTERSEA GENERAL HOSPITAL, Battersea Park,** S.W.11. SURGICAL OFFICER, resident. Junior Hospital Medical Officer grade. Vacant 8th May, 1958.

Apply Hospital Secretary, enclosing copies of 2 recent testimonials.

**BOLINGBROKE HOSPITAL, Wandsworth Common,** S.W.11. HOUSE SURGEON, resident. Vacant 18th May, 1958. Open to registered practitioners and pre-registration candidates.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 21st April, 1958.

**BROMPTON HOSPITAL, S.W.3. Applications are invited** for the post of Part-time RADIOLOGICAL REGISTRAR for attendance up to 4 sessions weekly, for 1 year in the first instance. Candidates are required to hold a Diploma in Diagnostic Radiology.

Applications, stating age, qualifications with dates, nationality and appointments held, accompanied by copies of 3 testimonials, by 3rd May to KENNETH A. F. MILES, House Governor.

**BROMPTON HOSPITAL, S.W.3. Applications invited** for post of SENIOR REGISTRAR (whole-time) to the Cardiac Department from those who have completed at least the third year of their general medical training as a Senior Registrar. One who has completed or will shortly be completing the fourth year is preferred. Applicants from the Commonwealth of Senior Registrar status are eligible provided they intend to return abroad on completion of training. Appointment is for 1 year with eligibility for reappointment.

Applications, stating age, qualifications with dates, nationality and appointments held, together with copies of 3 testimonials, by 3rd May, 1958, to KENNETH A. F. MILES, House Governor.

**CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10.** Pre-registration RESIDENT HOUSE OFFICER required in Obstetrics and Gynæcology. Post recognised for D.Obst.R.C.O.G. and M.R.C.O.G. examinations. Pre-registration candidates only will be considered. Post vacant 20th May.

Applications, with 2 testimonials, to Medical Director by 26th April, 1958.

**CHILDREN'S HOSPITAL, Sydenham, S.E.26. Senior** RESIDENT MEDICAL OFFICER (Senior House Officer) required for 1 year. Duties include medicine and surgery. Recognised for D.C.H. Previous pædiatric experience essential.

Apply, naming 2 referees, to Administrative Officer by 23rd April.

**CHILDREN'S HOSPITAL, Sydenham, S.E.26. House** OFFICER (medicine and surgery) required 29th April. Recognised for D.C.H.

Apply immediately, naming 2 referees, to the Administrative Officer.

**DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich,** S.E.10. HOUSE PHYSICIAN (pre-registration) required on 1st June.

Applications, stating age, nationality, qualifications and experience, with the names of 3 recent referees, should be sent to the Secretary at the above address not later than 1st May.

**DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich,** S.E.10. HOUSE SURGEON (pre-registration) required immediately.

Applications, stating age, nationality, qualifications and experience, and giving the names of 3 recent referees, should be sent to the Secretary at the above address as soon as possible.

**ELIZABETH GARRETT ANDERSON HOSPITAL,** Euston-road, N.W.1 (ROYAL FREE HOSPITAL GROUP). Applications are invited from registered Women medical practitioners for the post of RESIDENT PATHOLOGIST. Salary in accordance with Ministry of Health scale for Senior House Officers. The appointment is for 6 months in the first instance. Duties to commence as soon as possible.

Applications, with copies of 3 recent testimonials, should be sent to The Secretary, Elizabeth Garrett Anderson Hospital.

**FOREST GATE HOSPITAL, Forest-lane, E.7. Pre-**registration OBSTETRIC HOUSE OFFICER (second post) required for 6 months commencing 1st June, 1958. The appointment is recognised for training candidates for M.R.C.O.G. and D.Obst.R.C.O.G.

Applications, with names of 2 referees, to Hospital Secretary by 26th April, 1958.

**FOUNTAIN GROUP HOSPITAL MANAGEMENT COM-**MITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR PSYCHIATRIC REGISTRAR required for duty in the above Group, which comprises some 800 Beds for mental deficiency, mainly for children. There is an Outpatient Department and a considerable amount of teaching and research is done. Possession of D.P.M. or D.C.H., preferably with a higher medical qualification is desirable. Experience of children's diseases is an advantage. Candidates may visit the Hospital.

Application forms and further details from Secretary, Fountain Hospital, Tooting-grove, London, S.W.17. Completed application forms should reach the Secretary by 26th April, 1958.

**HACKNEY HOSPITAL, London, E.9. (General—857 Beds.)** Applications are invited for appointment as SENIOR HOUSE OFFICER (casualty). Vacant 10th June. The department is supervised by the Orthopædic Surgeon and the post can rotate with that of Senior House Officer (orthopædics).

Apply Group Secretary, above address, by 10th May, quoting HH/SHO.

**HACKNEY HOSPITAL, London, E.9. (General—857 Beds.)** Applications are invited for appointment as SENIOR HOUSE OFFICER (orthopædics). Vacant 10th June. The Senior House Officer works directly under the Consultant in a unit of 36 Beds; the post offers excellent experience, and is recognised for the F.R.C.S.

Apply Group Secretary, above, address, by 10th May, 1958.

**HAMMERSMITH HOSPITAL AND POSTGRADUATE** MEDICAL SCHOOL, Ducane-road, London, W.12. 2 Whole-time NON-RESIDENT SENIOR HOUSE OFFICERS required 1st October. These posts are for trainees in diagnostic radiology and are normally tenable for 1 year with a possibility of a second year. Higher medical or surgical qualifications would be an advantage.

Detailed applications, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London, and St. Mark's Hospitals, Ducane-road, London, W.12, by 10th May.

**HAMMERSMITH HOSPITAL AND POSTGRADUATE** MEDICAL SCHOOL, Ducane-road, London, W.12. Whole-time NON-RESIDENT SENIOR REGISTRAR (radiodiagnostic) required as soon as possible.

Detailed applications, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 3rd May.

**HAMMERSMITH HOSPITAL AND POSTGRADUATE** MEDICAL SCHOOL, Ducane-road, London, W.12. Whole-time NON-RESIDENT REGISTRAR (general surgery) required. Post vacant 6th June.

Detailed applications, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 30th April.

**HAMMERSMITH HOSPITAL AND POSTGRADUATE** MEDICAL SCHOOL, Ducane-road, London, W.12. RESIDENT HOUSE PHYSICIAN (pædiatrics) required 1st July. Post recognised for D.C.H.

Applications on forms obtainable from the Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, to be returned by 3rd May.

**HAMMERSMITH HOSPITAL AND POSTGRADUATE** MEDICAL SCHOOL, Ducane-road, London, W.12. 2 RESIDENT HOUSE SURGEONS (radiotherapy) required, one 1st July, one 5th July. These posts offer opportunities for attending general surgical postgraduate teaching.

Detailed applications, copies 2 recent testimonials, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 3rd May.

**HAMMERSMITH HOSPITAL AND POSTGRADUATE** MEDICAL SCHOOL, Ducane-road, London, W.12. RESIDENT HOUSE PHYSICIAN required 1st July for duties in tuberculosis wards and Hammersmith Chest Clinic dealing with all types of respiratory diseases.

Detailed applications, copies 2 recent testimonials, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 3rd May.

**HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60,** Grove End-road, London, N.W.8. Applications are invited from pre-registration or registered medical practitioners (Male) for the appointment of HOUSE SURGEON to become vacant on Friday, 23rd May, 1958. This post is recognised for purposes of the F.R.C.S. (Eng.). Appointment will be for a period of 6 months. National Health Service salary.

Applications should reach the Secretary on or before Saturday, 26th April together with copies of 3 recent testimonials.

**MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hamp-**stead, N.W.3. HAREFIELD AND NORTHWOOD GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT MEDICAL OFFICER (House Officer grade) required.

Applications, with copies of testimonials, to the Administrative Officer by 3rd May, 1958.

**MEMORIAL HOSPITAL, Shooters Hill, S.E.18. Senior** HOUSE OFFICER (anæsthetics), vacant 4th May. The post provides good experience and is recognised for F.F.A. R.C.S. and D.A. 6 months' resident appointment and may then be renewed.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

**MILE END HOSPITAL, Bancroft-road, London, E.1.** (479 Beds.) HOUSE PHYSICIAN (pre- or post-registration). Post vacant 10th May, 1958.

Applications forms, obtainable from Physician-Superintendent, to be returned by 2nd May, 1958, with copies of not more than 3 testimonials.

**LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST.** A vacancy occurs 1st June, 1958, for REGISTRAR in Clinical Pathology (Registrar grade). The appointment (resident) is a whole-time one and will be for 1 year in the first instance.

Applications, stating date of birth, qualifications with dates, and previous experience, together with copies of 3 testimonials, should reach the undersigned not later than 3rd May.

J. ROBBINS, House Governor.

London Chest Hospital, E.2.

**LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST.** 2 vacancies (1 resident, 1 non-resident) occur 1st June, 1958, for HOUSE PHYSICIAN. Appointment for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and post graded as House Officer. Duties include work in the Outpatient Department and special clinics as well as in wards. The resident post will be attached to the cardiological firm during the 4 months in London.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 3rd May.

J. ROBBINS, House Governor.

London Chest Hospital, E.2.

**LONDON CHEST HOSPITAL (Country Branch). Hospitals for Diseases of the Chest.** REGISTRAR in Clinical Pathology (Registrar grade). A vacancy occurs at the Country Branch, near Letchworth. The appointment is a whole-time one and will be for 1 year in the first instance, and the holder may be resident or non-resident.

Applications, stating age, qualifications with dates, and previous experience, together with copies of 3 testimonials, should be forwarded at once to J. ROBBINS, House Governor, London Chest Hospital, E.2.

**NATIONAL HOSPITALS FOR NERVOUS DISEASES.** Applications are invited from registered medical practitioners for the appointment of REGISTRAR (non-resident) at The National Hospital, Queen-square, W.C.1, for duty in the Outpatient Department and the Department of Applied Electro-Physiology. This post carries the grade of Registrar. The appointment will be for 1 year in the first instance.

Applications, with names of 3 referees, to be sent to the undersigned not later than 30th April, 1958.

H. EWART MITCHELL, Secretary to the Board of Governors.

The National Hospitals for Nervous Diseases,
Queen-square, London, W.C.1.

**NORTH MIDDLESEX HOSPITAL, London, N.18. House** PHYSICIAN (resident), post-registration, required for 1st June, for 6 months. General medicine.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 30th April.

**NORTH MIDDLESEX HOSPITAL, London, N.18. House** SURGEON (pre- or post-registration), resident, required for 1st June, for 6 months. Duties mainly general surgery, with some E.N.T. surgery. Post recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital by 30th April.

**PADDINGTON GREEN CHILDREN'S HOSPITAL, W.2.** (St. Mary's Hospital.) Applications are invited for the posts of :—

(*a*) HOUSE PHYSICIAN.
(*b*) HOUSE SURGEON.

Pre-registration posts, vacant 1st June, 1958. Tenable for 6 months.

Applications, stating age, nationality, qualifications with dates, and experience, with copies of 3 recent testimonials, should reach the Secretary not later than Saturday, 3rd May, 1958.

**PRINCE OF WALES'S GENERAL HOSPITAL, N.15.** Applications are invited for the appointment of RESIDENT PÆDIATRIC HOUSE PHYSICIAN (third post) to the above Hospital for a period of 6 months, vacant on 29th April, 1958 (post recognised for D.C.H.).

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned immediately.

**QUEEN MARY'S HOSPITAL FOR THE EAST END,** Stratford, E.15. HOUSE PHYSICIAN (third post) required to cover extra beds in process of being opened in General Medical Inpatient Department at Plaistow Hospital. Inpatient work only at present. 6 months' appointment to commence as soon as possible. Suitable for postgraduate study for higher diploma in medicine.

Apply to Hospital Secretary, giving names of 3 referees, by 26th April, 1958.

**QUEEN MARY'S HOSPITAL FOR THE EAST END,** Stratford, E.15. CASUALTY OFFICER (post-registration House Officer grade) required for 6 months commencing as soon as possible.

Applications, with the names of 3 referees, to Hospital Secretary by 26th April, 1958.

**ROYAL FREE HOSPITAL, W.C.1. Applications are invited** from registered medical practitioners for the post of RESIDENT ASSISTANT PATHOLOGIST (Senior House Officer). The post is for 1 year from 1st July, 1958. Salary and conditions of service as laid down by the Ministry of Health.

Application forms may be obtained from the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 5th May, 1958.

**ROYAL FREE HOSPITAL, W.C.1. Applications are** invited for the post of RESIDENT MEDICAL OFFICER to work at the Lawn Road Branch of the Royal Free Hospital. Terms and conditions of service in accordance with the Junior Hospital Medical Officer scale. The appointment is for 1 year in the first instance, to commence on 1st July, 1958.

Application forms may be obtained from the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 5th May, 1958.

**ROYAL FREE HOSPITAL, W.C.1. Applications are** invited for the post of RESIDENT MEDICAL OFFICER at the Royal Free Hospital. Terms and conditions of service in accordance with the Junior Hospital Medical Officer scale. The appointment is for 1 year in the first instance and commences on 1st July, 1958.

Application forms may be obtained from the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 5th May, 1958.

**ROYAL FREE HOSPITAL, W.C.1. Applications are invited** for the following posts :—

(*a*) 6 months HOUSE OFFICER, Infectious Diseases Department, followed by 6 months PÆDIATRIC HOUSE PHYSICIAN.
(*b*) 6 months PÆDIATRIC HOUSE PHYSICIAN, followed by 6 months HOUSE OFFICER, Infectious Diseases Department.

The posts are full-time, resident and are recognised pre-registration posts. Duties to commence on 1st July, 1958. Salary and conditions of service in accordance with those laid down by the Ministry of Health.

Application forms may be obtained from the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 5th May, 1958.

**ROYAL FREE HOSPITAL, W.C.1. Applications are invited** from registered medical practitioners for the post of SENIOR CASUALTY OFFICER at the Royal Free Hospital, Gray's Inn-road, W.C.1. The appointment is full-time, resident, for 6 months' duties to commence on 1st July, 1958. Salary and conditions of service in accordance with those laid down by the Ministry of Health for Senior House Officers.

Application forms may be obtained from the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 5th May, 1958.

**ST. ANN'S GENERAL HOSPITAL, N.15. Applications** are invited for the appointment of RESIDENT HOUSE SURGEON (third post) to above Hospital for a period of 6 months from 16th May, 1958.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15.

**ST. ANN'S GENERAL HOSPITAL, N.15. Applications** are invited for the appointment of RESIDENT HOUSE PHYSICIAN (Senior House Officer) to above Hospital for duty in the Infectious Diseases Unit and other general duties, for a period of 6 months from 22nd May, 1958.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 3rd May, 1958.

**ST. BARTHOLOMEW'S HOSPITAL, E.C.1. Applications** are invited for the post of Whole-time SENIOR HOUSE OFFICER or REGISTRAR to the Diagnostic Radiology Department. The post is tenable from 1st October, 1958, and is non-resident. The appointment made will depend on the qualifications and experience of the successful applicant.

Applications, together with the names of 2 referees, should be submitted to the undersigned within the next 7 days.

C. C. CARUS-WILSON, Clerk to the Governors.

**ST. GILES' HOSPITAL, Camberwell, S.E.5. House** SURGEON (orthopædic duties) required as Locum Tenens until 30th June in first instance. Pre- or post-registration.

Apply, giving personal details, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, East Dulwich Grove, S.E.22.

**ST. JAMES' HOSPITAL, Balham, London, S.W.12.** SENIOR HOUSE OFFICER (casualty), resident or non-resident. Vacant 6th June. Post recognised for F.R.C.S.

Applications, stating age, qualifications, experience, and names of 2 referees, to the Group Secretary, Wandsworth Hospital Group, at above address, by 3rd May.

**ST. JAMES' HOSPITAL, Balham, London, S.W.12.** Locum SENIOR HOUSE OFFICER (casualty) required from 22nd May to 5th June inclusive.

Applications, giving full details and names of 2 referees, to Group Secretary at above address by 30th April.

**ST. JAMES' HOSPITAL, Balham, London, S.W.12.** Locum REGISTRAR (anæsthetics) required from 1st to 8th May inclusive.

Applications, giving full details and names of 2 referees, to Group Secretary at above address immediately.

**ST. THOMAS'S HOSPITAL, London, S.E.1. Registrar** to the Children's Department. 1 year in the first instance from 18th May, 1958.

Applications, naming 2 referees, to the Clerk of the Governors by 28th April, 1958.

**ST. THOMAS'S HOSPITAL, London, S.E.1. Obstetric** HOUSE PHYSICIAN at the General Lying-In Hospital, York-road, S.E.1, for a period of 6 months from 1st July, 1958. Resident. Approved service for M.R.C.O.G.

Applications, naming 2 referees, from fully registered medical practitioners only, to Clerk of the Governors by 30th April, 1958.

**ST. THOMAS'S HOSPITAL, London, S.E.1. Senior** REGISTRAR to the Department of Anæsthetics. For a period of 1 year in the first instance. Whole-time.

Applications, naming 2 referees, to the Clerk of the Governors by 28th April, 1958.

**ST. MARY'S HOSPITAL, W.2. Registrar to the Pædiatric** Department at St. Mary's Hospital. Previous pædiatric experience necessary, preference given to holders of the M.R.C.P. The appointment will be for a first period of 12 months from 1st September, 1958. Successful candidate required to undertake duties in the St. Mary's Hospital Pædiatric Unit and at the constituent hospitals; may be eligible to participate in exchange scheme with Children's Medical Centre, Boston (Harvard University).

Applications, giving full details, with names and addresses of 3 referees, should reach the House Governor not later than 30th April, 1958.

**ST. MARY'S HOSPITAL, Paddington, W.2. Resident** HOUSE PHYSICIAN to the Neurological, Dermatological and Venereological Departments, for 6 months from 1st June, 1958. Second pre-registration or post-registration candidates are eligible to apply.

Applications, giving full details, names and addresses of 3 referees, to reach the House Governor, by 28th April, 1958.

**ST. MARY'S HOSPITAL, Paddington, W.2. Senior** REGISTRAR to the Orthopædic Department at St. Mary's Hospital. Higher qualification essential. The appointment will be for a first period of 12 months, from 1st June, 1958.

Applications, giving full details, with names and addresses of 3 referees, should reach the House Governor not later than 5th May, 1958.

**THE HOSPITAL FOR SICK CHILDREN, Great Ormond-**street, London, W.C.1. There will be a vacancy on 3rd July, 1958, for a RESIDENT E.N.T. REGISTRAR (Registrar grade).

Further particulars and form of application, which must be returned not later than 12th May, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Govenor and Secretary.

**THE HOSPITAL FOR SICK CHILDREN, Great Ormond-**street, London, W.C.1. There will be vacancies on 15th July, 1958, for the following SENIOR HOUSE OFFICERS:—

2 House Physicians.
2 House Surgeons.

Further particulars and form of applications, which must be returned not later than 12th May, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

**THE HOSPITAL FOR SICK CHILDREN, Great Ormond-**street, London, W.C.1. There will be a vacancy on 22nd July, 1958, for a JUNIOR ANÆSTHETICS REGISTRAR (Senior House Officer grade).

Further particulars and form of application, which must be returned not later than 12th May, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

**WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.)** Applications are invited for the post of OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON, vacant 22nd May, 1958. The appointment is recognised for D.Obst.R.C.O.G.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

**WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1.** Applications invited for post of SENIOR REGISTRAR to Radiological (Diagnostic) Department for 1 year in first instance from 1st July, 1958.

Applications (12 copies), with names of 2 referees, to House Governor by 3rd May.

**WHIPPS CROSS HOSPITAL, London, E.11. Applications** are invited for the post of HOUSE SURGEON in the Orthopædic Department (post- or pre-registration). This post, which is recognised for the F.R.C.S., is vacant now.

Applications forms from the Hospital Secretary, to be returned within 10 days of the appearance of this advertisement.

**WHIPPS CROSS HOSPITAL, London, E.11. Leyton-**STONE (No. 10) HOSPITAL GROUP. Applications are invited for the post of SENIOR HOUSE OFFICER (pathology) at the Area Laboratory at above Hospital. The post is normally a resident one but applications will be considered from persons wishing to be non-resident, providing that they will reside near the Hospital and be on call.

Application forms obtainable from the Hospital Secretary, to be returned by 28th April, 1958.

**ABERYSTWYTH, CARDIGANSHIRE. GENERAL HOS-**PITAL. MID-WALES HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (surgical) required (resident). Post recognised for F.R.C.S. examination. Vacancy immediate.

Applications, stating age, experience, &c., to the Group Secretary, Mid-Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cardiganshire.

**ALEXANDRIA, DUNBARTONSHIRE. VALE OF LEVEN** HOSPITAL. BOARD OF MANAGEMENT FOR DUNBARTONSHIRE HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER in Surgery and Gynæcology at the above Hospital. This post may now be held by applicants who have done 2 pre-registration House posts.

Applications, together with the names of 2 referees, to be submitted immediately to the Medical Superintendent at the Hospital.

**ALTON, HAMPSHIRE. LORD MAYOR TRELOAR** ORTHOPÆDIC HOSPITAL. Applications are invited from registered medical practitioners for the post of Whole-time ORTHOPÆDIC REGISTRAR. Post provides experience in non-pulmonary tuberculosis and general orthopædics, and includes attendances at peripheral clinics. It is recognised for 6 months' training under F.R.C.S. regulations. The post is resident for married or single persons. Canvassing disqualifies, but visit to Hospital welcomed.

Write to the Secretary for application form.

**ALTON, HAMPSHIRE. LORD MAYOR TRELOAR** ORTHOPÆDIC HOSPITAL. Locum ORTHOPÆDIC REGISTRAR required probably for 2 or 3 months. Post provides experience in non-pulmonary tuberculosis and general orthopædics and includes attendances at peripheral clinics. Residence available.

Apply as soon as possible, with names of 2 referees, to the Secretary, Lord Mayor Treloar Orthopædic Hospital, Alton, Hants.

**ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGE-**MENT COMMITTEE. 2 HOUSE SURGEONS required at Ashton-under-Lyne General Hospital. Preference will be given to pre-registration applicants. Recognised for F.R.C.S.(Eng.). Vacant May.

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne.

**ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGE-**MENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER (resident) required for Casualty Department, Ashton-under-Lyne General Hospital. Appointment limited to 4 years. Minimum commencing salary £852 10s. p.a. but higher salary may be paid according to experience and qualifications. There may be some orthopædic duties to be undertaken by the holder of this post. Recognised under F.R.C.S. regulations.

Apply, giving age, experience, qualifications and 2 references, to Group Secretary, General Hospital, Ashton-under-Lyne.

**ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.)** STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE SURGEONS (2) for Traumatic and Orthopædic Unit. 6-month appointments, suitable for pre-registration candidates.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital immediately.

**BARNSTAPLE. NORTH DEVON INFIRMARY. (105** Beds.) SENIOR HOUSE OFFICER required, whose duties will be mainly casualty. The post is tenable for 1 year, and will be vacant in early June. Small furnished flat available.

Applications to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

**BARROW-IN-FURNESS. NORTH LONSDALE HOS-**PITAL. Applications are invited for the resident post of HOUSE OFFICER (surgical) (approved for pre-registration) at the North Lonsdale Hospital, Barrow-in-Furness. Post available immediately. Recognised for F.R.C.S.

Applications to the Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey-road, Barrow-in-Furness.

**BARRY ACCIDENT AND SURGICAL HOSPITAL.** SENIOR HOUSE OFFICER required. Unfurnished house available to rent.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

**BATLEY, THE GENERAL HOSPITAL. (99 Beds.)** RESIDENT SENIOR HOUSE OFFICER (ophthalmology and E.N.T.). This appointment is recognised for the Diploma in Ophthalmology and, in addition to work at the above Hospital, the person appointed will be required to carry out certain clinical duties at other hospitals in the Group. The post will be vacant early in May, 1958.

Applications should be sent forthwith to the Administrative Officer, The General Hospital, Carlinghow, Hill, Batley, Yorks.

**BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS** AND ESSEX GENERAL HOSPITAL. Applications invited for post of HOUSE OFFICER (surgical) (pre-registration). Salary £467 10s.–£522 10s. p.a. less £125 for residential emoluments. Appointment to commence 21st April, 1958.

Applications, stating age, nationality, qualifications and experience with copies of 2 recent testimonials or names of referees, to Hospital Secretary.

**BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, Birm-**INGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEON (resident). Hospital largest traumatic unit in the country and treats over 50,000 new patients each year. Recognised for purpose of casualty by R.C.S. (Eng.). Teaching programme by Consultant staff. 6-month appointment, some of which may be spent in 42-bedded Medical Research Council's Burns Unit.

Apply, naming 2 referees, to Administrator.

**BIRMINGHAM (near). MIDLAND CENTRE FOR** NEUROSURGERY, Holly-lane, SMETHWICK, near BIRMINGHAM. RESIDENT SENIOR HOUSE OFFICERS, vacant in July. Recognised for period of 6 months' unspecified training under R.C.S. regulations. This is a new hospital, entirely devoted to neurology and neurosurgery, within easy reach of Birmingham. Salary on national scale less deduction for board, lodging, &c.

Applications, with names of 2 referees, to the Group Secretary, West Bromwich and District Hospitals Management Committee.

**BIRMINGHAM REGIONAL HOSPITAL BOARD.**

**Birmingham (Selly Oak) Group, Oak Tree-lane, Birmingham, 29**

(1) REGISTRAR (ophthalmology). Duties Selly Oak Eye Department and Little Bromwich General Hospital. Recognised for D.O. and F.R.C.S.(Eng.).

**Birmingham (Sanatoria) Group, Yardley Green Hospital, Birmingham, 9**

(2) REGISTRAR (chest diseases and tuberculosis). Romsley Hill Hospital (136 Beds, including Diabetic Unit), Romsley, Halesowen, Birmingham. Duties also at Birmingham Chest Clinic. Accommodation for single person available.

**Coventry No. 20 Group, Coventry and Warwickshire Hospital, Coventry**

(3) REGISTRAR (general surgery). Coventry and Warwickshire Hospital, Coventry (354 Beds). Resident. Recognised F.R.C.S. Experience in specialty essential. Higher qualification desirable.

Application forms from Group Secretaries, to be returned by 28th April, 1958.

**BIRMINGHAM, 29. SELLY OAK HOSPITAL. (1033** equipped Beds.) ASSISTANT CASUALTY OFFICER (Senior House Officer). Resident/non-resident. Recognised for F.R.C.S.

Applications, giving qualifications, experience, age, and copies of 3 recent testimonials, should be sent to the Medical Superintendent.

**BIRMINGHAM. THE UNITED BIRMINGHAM HOS-**PITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade). Post vacant 12th June, 1958. The post is suitable for persons training for pædiatrics or contemplating a career in pathology. The holder is expected to attend clinical rounds and meetings and to assist in the investigation of clinical problems.

Forms of application, obtainable from the House Governor, should be returned to him by 30th April, 1958.

G. A. PHALP, Secretary to the Board of Governors.

**BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS.** THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the appointment of RESIDENT MEDICAL OFFICER in the grade of Senior House Officer, vacant 7th July, 1958, for 1 year.

Forms of application may be obtained from the House Governor and should be returned to him not later than 30th April, 1958.

G. A. PHALP, Secretary to the Board of Governors.

**BLACKBURN. QUEEN'S PARK HOSPITAL.** House PHYSICIAN required immediately. Post recognised for pre-registration purposes.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

**BLACKPOOL VICTORIA HOSPITAL. (354 Beds.)** Senior HOUSE OFFICER (casualty and traumatic surgery). Recognised for F.R.C.S. and offering wide variety of experience. Post now vacant.

Applications, stating age, experience and qualifications and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

**BLACKPOOL VICTORIA HOSPITAL. (354 Beds.)** House PHYSICIAN. Resident pre-registration post, vacant on 12th May, 1958.

Applications, stating age, experience (if any), and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

**BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.**

**The Royal Infirmary, Bolton** (238 Beds)

SENIOR HOUSE OFFICER (resident or non-resident) for Casualty Department with some orthopædic duties. Now vacant, tenable for 12 months. Recognised for F.R.C.S. Staff of 2 with Consultant supervision and adequate relief. Post offers good casualty/accident experience.

**Bolton District General Hospital** (607 Beds)

RESIDENT HOUSE SURGEON. Now vacant, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

**BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE.** HOUSE PHYSICIANS (pre-registration) required for Poole General Hospital on 23rd May, 1958, and for Poole General and Alderney Hospitals on 19th May, 1958.

Applications to the Hospital Secretary.

**BOURNEMOUTH. ROYAL VICTORIA HOSPITAL,** Shelley-road, BOSCOMBE. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of HOUSE PHYSICIAN. The appointment, which becomes vacant on 14th June, 1958, is recognised for pre-registration purposes.

Applications to the Hospital Secretary.

**BOURNEMOUTH. ROYAL VICTORIA HOSPITAL,** Shelley-road, BOSCOMBE. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the immediate appointment of SENIOR HOUSE OFFICER (resident or non-resident—orthopædics and casualty combined). The post is recognised for the F.R.C.S. examination and is normally tenable for 12 months. The Unit consists of a Registrar and 2 Senior House Officers with an additional Senior House Officer during the summer months.

Applications to the Hospital Secretary.

**BOURNEMOUTH. ROYAL VICTORIA HOSPITAL,** Shelley-road, BOSCOMBE. (494 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the immediate appointment of 2 HOUSE SURGEONS. The appointments are recognised for the F.R.C.S. examination and for pre-registration purposes.

Applications to the Hospital Secretary.

**BRADFORD ROYAL INFIRMARY. (507 Beds.)** House SURGEONS required for the post of General Surgery and General Surgery/Urology. Both posts recognised for F.R.C.S. and pre-registration purposes. Vacant 1st May, 1958.

Applications, stating age, qualifications, experience and nationality, with copy testimonials, to Secretary.

**BRADFORD. ST. LUKE'S HOSPITAL. (724 Beds.)** HOUSE SURGEON (general surgery/plastic) required for 1st May, 1958. Recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, experience, and nationality, with copy testimonials, to Secretary, Bradford Royal Infirmary.

**BRADFORD. ST. LUKE'S HOSPITAL. (724 Beds.)** House PHYSICIAN (pædiatrics) required for 1st May, 1958. Recognised for pre-registration purposes.

Applications, stating age, qualifications, experience and nationality, with copy testimonials, to Secretary, Bradford Royal Infirmary.

**BRADFORD, YORKSHIRE. THE ROYAL EYE AND EAR HOSPITAL.** (105 Beds.) SENIOR HOUSE OFFICER required for Ear, Nose, and Throat Department of 56 Beds. Recognised for D.L.O. and F.R.C.S. Post vacant 27th May, 1958. Salary £819 10s. p.a., less £150 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to the Secretary, Royal Infirmary, Bradford, 9.

**BURTON-ON-TRENT. THE GENERAL HOSPITAL.** HOUSE OFFICER (orthopædics) (pre-registration post) required at the above Hospital. Recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

**BURTON-ON-TRENT. THE GENERAL HOSPITAL.** JUNIOR HOSPITAL MEDICAL OFFICER (casualty and orthopædics), resident or non-resident, required at the above Hospital. Furnished or unfurnished flat available for married applicant.

Applications to Group Secretary as soon as possible.

**BRIGHTON GENERAL HOSPITAL. Brighton and LEWES HOSPITAL MANAGEMENT COMMITTEE.** SENIOR HOUSE OFFICER for General Surgical Unit (60 Beds). Vacant 25th May, 1958. Recognised for F.R.C.S. and offers considerable scope for operative surgery. Salary in accordance with national scale.

Applications, stating age, qualifications and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7.

**BRIGHTON GENERAL HOSPITAL.** Applications are invited for the appointment of HOUSE SURGEON to the Orthopædic Unit. Salary in accordance with national scale. This is a pre-registration appointment.

Applications, stating age, qualifications and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

**BROXBURN, WEST LOTHIAN. BANGOUR GENERAL HOSPITAL.** (15 miles from Edinburgh.) SENIOR HOUSE OFFICERS required immediately for General Surgical Department of Bangour General Hospital. The Hospital is a large general hospital with the following departments: General Surgery, Plastic Surgery, Neurosurgery, E.N.T., Oral Surgery, Ophthalmology, Maternity, General Medicine, Pneumoconiosis, Tuberculosis and Chest. Salary and conditions of service in accordance with regulations.

Applications should be made to The Group Secretary and Treasurer, Board of Management, Bangour General Hospital, Broxburn, West Lothian.

**BURY ST. EDMUNDS. WEST SUFFOLK GENERAL HOSPITAL.** (262 Beds.)

(*a*) SENIOR HOUSE OFFICER or HOUSE OFFICER (orthopædic and casualty duties); post recognised for F.R.C.S. (surgical); vacant late April.

(*b*) HOUSE PHYSICIAN (pædiatric and general medical duties); vacant late May.

(*c*) HOUSE PHYSICIAN (general medical duties); vacant early June.

(*d*) HOUSE SURGEON (general surgical duties), recognised for F.R.C.S. (surgical); vacant late June.

(*e*) HOUSE SURGEON (general surgical and other duties); vacant late May.

(*f*) HOUSE SURGEON (obstetric and gynæcological duties), recognised for D.Obst.R.C.O.G., vacant early July.

Except Senior House Officer, all posts recognised for pre-registration purposes.

Applications, with testimonials or names of referees, to Hospital Secretary.

**CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS.** SENIOR HOUSE OFFICER (Resident), Maternity Hospital, Cambridge. Vacant from May for 6 months in first instance with possible extension to 1 year. Some previous obstetrical experience essential. Recognised obstetrical appointment for M.R.C.O.G. and D.Obst.R.C.O.G.

Apply immediately, stating age, nationality, qualifications and experience with dates, and with copies of 3 testimonials, to Secretary, United Cambridge Hospitals, Addenbrooke's Hospital, Cambridge.

**CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS.** ADDENBROOKE'S HOSPITAL, CAMBRIDGE. ANÆSTHETIC SENIOR HOUSE OFFICER (resident) for 1 year from 1st June. Anæsthetic experience essential. Recognised for D.A. and F.F.A. R.C.S.

Apply to the Secretary by 26th April, stating age, nationality, qualifications and experience with dates, and copies of 3 testimonials. Interviews early May.

**CANTERBURY. KENT AND CANTERBURY HOSPITAL.** (277 Beds.) The post of SENIOR HOUSE PHYSICIAN is now vacant at Stodmarsh Road Annexe. Duties include care of 30-Bedded unit of chest diseases, also work at the Chest Clinic and with the Pneumoconiosis Unit. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

**CANTERBURY. KENT AND CANTERBURY HOSPITAL.** (277 Beds.) The post of GENERAL SURGICAL AND UROLOGICAL HOUSE SURGEON (pre-registration or third post), which is recognised for the F.R.C.S., is now vacant. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

**CARDIFF. THE UNITED CARDIFF HOSPITALS.** Applications are invited for the appointment of SENIOR REGISTRAR in General Surgery at the Cardiff Royal Infirmary. Non-resident appointment, to commence July, 1958.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned with 14 days of the appearance of this advertisement.

**CARDIFF. THE UNITED CARDIFF HOSPITALS.** Applications are invited for the appointment of SENIOR REGISTRAR in General Medicine at the Cardiff Royal Infirmary, to commence duty as soon as possible.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

**CARDIFF. THE UNITED CARDIFF HOSPITALS.** Applications are invited for the appointment of SENIOR HOUSE OFFICER in the Casualty/Orthopædic and Fracture Departments at the Cardiff Royal Infirmary. Non-resident post. Recognised for F.R.C.S. The successful candidate will spend 4 months of the appointment in the Orthopædic/Fracture Department, and 8 months in the Casualty Department.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

**CARDIFF. THE UNITED CARDIFF HOSPITALS.** Applications are invited for the appointment of Locum SENIOR HOUSE OFFICER in the Department of Pathology at Llandough Hospital for 3 months from 1st May to 31st July, 1958. Resident post.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

**CARDIFF. GLAN ELY HOSPITAL, Fairwater,** CARDIFF. There will be a vacancy for a SENIOR HOUSE OFFICER early in April in this Hospital, which has 240 Beds for the treatment of tuberculosis—both pulmonary and non-pulmonary—and allied chest conditions. Experience available in thoracic surgery and operative treatment of bone and joint, genitourinary, and glandular tuberculosis.

Form of application from Group Secretary, 44, Cathedral-road, Cardiff.

**CARDIFF HOSPITAL MANAGEMENT COMMITTEE.** SENIOR HOUSE OFFICER (surgical) required at Rookwood Hospital.

Form of application from Group Secretary, 44, Cathedral-road, Cardiff.

**CARLUKE, LANARKSHIRE. LAW HOSPITAL. (790** Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (medical).

Applications, stating age, qualifications and previous experience, together with the names of 2 referees, should be sent to the Group Medical Superintendent.

**CARSHALTON, SURREY. ST. HELIER HOSPITAL.** HOUSE SURGEON (approved for pre-registration service). General surgery with duties in E.N.T. Vacant 12th May.

Applications, giving age, qualifications, &c., with copies of recent testimonials or the names and addresses of 2 referees, should be sent to the Secretary at the above address.

**CHELMSFORD AND ESSEX HOSPITAL. Resident** Locum Tenens REGISTRAR in Surgery required to work at the above Hospital for period 28th April–16th May.

Applications to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

**CHELMSFORD. ST. JOHN'S HOSPITAL. Applications** are invited from registered practitioners for the post of RESIDENT PÆDIATRIC HOUSE OFFICER (Male or Female) commencing as soon as possible. To work in the Pædiatric Unit of the Chelmsford Hospital Group. The Unit includes a premature baby nursery of 10 cots and a Neonatal Department in the Maternity Block of the Hospital. The Department is recognised for the D.C.H.

Applications, stating age, nationality, qualifications and experience, together with recent testimonials, should be forwarded immediately to the Group Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

**CHERTSEY, SURREY. ST. PETER'S HOSPITAL.** (430 Beds.) RADIOLOGICAL REGISTRAR. 1 of the 2 Registrar posts in the Diagnostic X-ray Department will become vacant shortly. Applicants must possess at least the D.M.R. (D) Part I.

Application forms may be obtained from the Group Secretary, Woking and Chertsey Hospital Management Committee, Huntington, Guildford-road, Chertsey, Surrey. Closing date 2nd May. The Department may be visited by arrangement with the Senior Radiologist (Ottershaw 441). Hospital within easy reach of London.

**COLCHESTER GROUP HOSPITAL MANAGEMENT** COMMITTEE. Applications invited for:—

**Black Notley Hospital, Braintree, Essex** (522 Beds)

Post of HOUSE OFFICER (orthopædic surgery). Duties include care of cases from London Hospital Orthopædic Department. Pre-registration or third post, tenable for 6 months. Recognised for F.R.C.S.

Post of Locum Tenens HOUSE SURGEON. Required immediately. Pre-registration or third post. Includes duties in general surgical and gynæcological wards. Recognised for F.R.C.S.

**Harwich and District Hospital, Dovercourt, Essex** (30 Beds)

Post of SENIOR HOUSE OFFICER. Duties include medical, surgical and casualty work.

**St. Mary's Hospital, Pope's-lane, Colchester**

Post of SENIOR HOUSE OFFICER (Resident Medical Officer) for Geriatric Unit, includes duties in connection with medical and surgical patients accommodated at hospital and duties at Essex County Hospital (general medical). Post tenable for 6 or 12 months. Resident.

**Essex County Hospital, Colchester, Essex** (181 Beds)

Post of HOUSE OFFICER to E.N.T. and Pædiatric Departments. Post tenable for 6 months. Post-registration appointment. Recognised for D.L.O. The Pædiatric Department consists of a new unit of 24 Beds.

Post of Locum SENIOR HOUSE OFFICER (anæsthetics) required from 20th May for approximately 2 months.

**Clacton and District Hospital, Clacton-on-Sea, Essex** (58 Beds)

REGISTRAR (temporary) required as Resident Casualty Officer during summer for period not exceeding 6 months.

Applications, with copies of 3 testimonials, to Secretary, Colchester Group Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

**COTTINGHAM. CASTLE HILL SANATORIUM (221** Beds) and RAYWELL SANATORIUM, near COTTINGHAM (48 Beds). RESIDENT SENIOR HOUSE OFFICER to work under supervision of Consultant Chest Physician in Group Sanatoria with Major Thoracic Surgery Unit and Mass Radiography and laboratory facilities.

Application forms from Group Secretary, Hull B Group Hospital Management Committee, De la Pole Hospital, Willerby, E. Yorkshire.

**CHICHESTER. ROYAL WEST SUSSEX HOSPITAL.** (202 acute beds.) RESIDENT HOUSE SURGEON required for 6 months' appointment. National salary scales for either provisionally or fully registered practitioners. Post approved for pre-registration practitioners and F.R.C.S. 8 residents. Vacant 8th May.

Applications, stating age, experience, qualifications with references or names of referees, to Senior Administrative Officer.

**CUCKFIELD HOSPITAL, Cuckfield, near Haywards** HEATH. RESIDENT JUNIOR HOUSE SURGEON (general surgery). Pre-registration post vacant early May. Tenable 6 months. Health Service conditions.

Applications, stating age, nationality and experience, with names of 2 referees, to Group Secretary, Mid-Sussex Hospital Management Committee.

**DERBY. DERBYSHIRE ROYAL INFIRMARY. (416** Beds.) SENIOR HOUSE OFFICER (general surgery) or HOUSE SURGEON (pre-registration). Resident. Appointment from 1st June for 6 months. Recognised for F.R.C.S.

Applications, stating full details and 2 names for reference, to Secretary.

**DERBY. DERBYSHIRE ROYAL INFIRMARY. (396 Beds.** Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (orthopædics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 28th April, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

**DEVONPORT. SOUTH DEVON AND EAST CORNWALL** HOSPITAL.

SENIOR HOUSE OFFICER in Surgery, vacant 1st June, 1958.

HOUSE SURGEON, pre-registration post, vacant 1st June, 1958.

Both recognised for the F.R.C.S.

Apply, with names of 3 referees, to the Group Secretary, 7, Nelson-gardens, Devonport.

**DEWSBURY. STAINCLIFFE GENERAL HOSPITAL,** Healds-road. (304 Beds.) The pre-registration appointment of HOUSE OFFICER (general surgery) is now vacant.

Applications, with full details, should be sent to the Administrative Officer at the Hospital.

**DEWSBURY. THE GENERAL HOSPITAL, Moorlands-**road. (128 Beds.) The pre-registration appointment of HOUSE OFFICER (general medicine and dermatology) falls vacant on 30th April, 1958.

Applications, giving full details, should be sent to the Administrative Officer at the Hospital.

**DONCASTER ROYAL INFIRMARY. (330 Beds.) Appli**cations are invited for the post of HOUSE SURGEON (Intern or Senior House Officer). Post recognised for F.R.C.S. Vacant early May.

Applications, with particulars of experience and copies of 2 recent testimonials, to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary.

**DORKING GENERAL HOSPITAL. (252 Beds.) Applica**tions are invited for the position of MEDICAL REGISTRAR to the Department of Medicine (40 acute medical beds), to commence duties on 1st June. The medical firm consists of a visiting Consultant Physician, a Medical Registrar (present post), and a Senior House Physician. Applicants should have had previous experience in general medicine and should for preference hold a higher qualification in medicine. There are unique opportunities for obtaining wide experience in all branches of medicine and in clinical research. The successful candidate must reside in or near the Hospital.

Application forms obtainable from Group Secretary, Redhill Hospital Management Committee, Earlswood Mount, Pendleton-road, Redhill, Surrey, and returnable within 14 days of advertisement.

**DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL** HOSPITAL. (247 Beds.) JUNIOR HOUSE PHYSICIAN required early May. Approved pre-registration post, but fully registered practitioners may apply. Duties to include geriatrics and acute medicine. Good general experience for first house appointment.

Apply Group Secretary, Westwood Hospital, Beverley, Yorkshire.

**DUMFRIES. CRICHTON ROYAL MENTAL HOSPITAL.** Applications are invited for the post of SENIOR HOUSE OFFICER. Salary according to national scale. Previous experience in psychiatry not required. Every facility for training in psychiatry on the most modern lines.

Forms of application to be obtained from the Physician-Superintendent, to whom these should be returned with copies of testimonials.

**DUNDEE (near). WESTGREEN MENTAL HOSPITAL.** (Teaching School for Queen's College, St. Andrews University.) Appointment of JUNIOR HOSPITAL MEDICAL OFFICER. Salary according to national scale. House in grounds is available for married man at appropriate rental. Ample opportunities for study and research.

Applications, stating age, nationality, qualifications and experience, with recent testimonials, should be sent to the Physician-Superintendent.

**EDGWARE GENERAL HOSPITAL, Edgware, Middlesex.** 2 OBSTETRIC HOUSE SURGEONS for above Hospital. Posts vacant 9th and 23rd May, 1958. 6 months' appointments. Posts recognised for M.R.C.O.G. purposes.

Applications, stating age, qualifications and experience, and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 25th April, 1958.

**EDGWARE GENERAL HOSPITAL, Edgware, Middlesex.** (647 Beds.) RESIDENT HOUSE PHYSICIAN for above Hospital. Post vacant 1st June, 1958. 6 months' appointment.

Applications, stating age, qualifications and experience, and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 2nd May, 1958.

**EDGWARE GENERAL HOSPITAL, Edgware, Middlesex.** (647 Beds.) RESIDENT HOUSE SURGEON (general and genitourinary) for above Hospital. Post vacant 18th May, 1958. 6 months' appointment. Post recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications and experience, and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 2nd May, 1958.

**EAST ANGLIAN REGIONAL HOSPITAL BOARD.** ORTHOPÆDIC REGISTRAR, Norfolk and Norwich Hospital (441 Beds.) Post provides excellent training. Appointment for 1 year renewable for second year.

Applications, stating age, experience and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 5th May, 1958. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

**EDINBURGH NORTHERN GROUP OF HOSPITALS.** SENIOR HOUSE OFFICER required for Department of Radiotherapy, Western General Hospital.

Applications, giving the names of 2 referees, to the Medical Superintendent, Western General Hospital, Edinburgh, 4.

**EDINBURGH. ROYAL HOSPITAL FOR SICK CHILDREN.** Applications are invited from registered medical practitioners and pre-registration graduates for 3 resident appointments of HOUSE PHYSICIAN for 6 months commencing 1st October, 1958. National Health Service scales.

Applications, stating age, qualifications and experience, with names of 2 referees, to be received not later than 2nd May by the Secretary, Edinburgh Central Hospitals, 1, Rillbank-terrace, Edinburgh, 9.

**ENFIELD. WAR MEMORIAL HOSPITAL, Chase Side,** ENFIELD, MIDDLESEX. RESIDENT SENIOR HOUSE OFFICER required immediately for general medical and surgical duties in acute general hospital of 61 Beds. 12 months' appointment.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

**EPPING. ST. MARGARET'S HOSPITAL. Senior House** OFFICER (anæsthetics) required. Resident. Post vacant early May. Busy general hospital; easy access to London. Good experience. Post recognised for D.A.

Applications, with copies of recent testimonials, to be sent to the Group Secretary, Epping Group Hospital Management Committee, Oak Cottage, The Plain, Epping, Essex, by 24th April.

**EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom,** SURREY. RESIDENT HOUSE SURGEON required 11th June, pre-registration post recognised for F.R.C.S.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

**EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom,** SURREY. RESIDENT HOUSE PHYSICIAN required 8th June. Fully registered post.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary, at above address.

**EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom,** SURREY. SENIOR HOUSE OFFICER (casualty) required 1st May. Non-resident post recognised for F.R.C.S. 12-month appointment. Busy Casualty and Outpatient Departments with excellent experience in minor and traumatic surgery. Candidates should have held previous House Officer posts.

Applications, stating age, qualifications, experience, with copies of 2 recent testimonials, should be sent immediately to Group Secretary at above address.

**EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom,** SURREY. RESIDENT HOUSE PHYSICIAN required 6th June. Pre-registration post.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent by 30th April to Group Secretary at above address.

**EXETER. ROYAL DEVON AND EXETER HOSPITAL.** Applications are invited from pre-registration and registered medical practitioners for the posts of HOUSE SURGEON (general surgery) (2). Vacant on 16th and 18th May, 1958, respectively.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary.

**GLASGOW, N.1. FORESTHALL HOSPITAL. (600 hos**pital beds for long-term sick.) JUNIOR HOSPITAL MEDICAL OFFICER. Applicants must have been qualified for 2 years and have had experience as House Officers in general hospitals. The present establishment is for 5 Junior Hospital Medical Officers and they are encouraged to spend part of their time at a nearby teaching hospital to maintain their interest in general medicine. Facilities and supervision are also provided for Medical Officers wishing to pursue clinical research in preparation for higher degrees. Living-in optional.

Applications, with the names of 3 referees, should be sent to the Administrative Medical Officer, Foresthall, 657, Edgefauld-road, Glasgow, N.1.

**GRANTHAM AND KESTEVEN GENERAL HOSPITAL.** (117 Beds. Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required, 7th May. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 28th April, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

**GUILDFORD. ROYAL SURREY COUNTY HOSPITAL.** RESIDENT HOUSE PHYSICIAN required from 19th May. Post is tenable for 6 months and recognised for pre-registration candidates.

Applications, with copies of 3 testimonials, to be sent to the Hospital Secretary as soon as possible.

**GUILDFORD. ROYAL SURREY COUNTY HOSPITAL.** Locum Tenens HOUSE SURGEON required 1st or 10th–24th May, for general surgery.

Applications, with full particulars and copies of testimonials, to Hospital Secretary as soon as possible. Telephone Guildford 2323.

**GUILDFORD. ROYAL SURREY COUNTY HOSPITAL.** RESIDENT HOUSE SURGEON required for General Surgery. Vacant early May and tenable for 6 months. It is approved for pre-registration candidates and also recognised for the F.R.C.S. examination.

Applications, with copies of 3 testimonials, should be sent to the Hospital Secretary.

**HAREFIELD HOSPITAL, Harefield, Middlesex. Applica**tions are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer) for duties on the Thoracic Surgical Unit.

Applications, together with copies of 2 testimonials, to be sent to the Medical Director, Harefield Hospital, Harefield, Middlesex, by 24th April, 1958.

**HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150** Beds.) HOUSE SURGEON (urology and ophthalmics) required. Pre-registration post vacant 1st June, 1958.

Apply to Hospital Administrator.

**HEMEL HEMPSTEAD, HERTFORDSHIRE. ST. PAUL'S** HOSPITAL. HOUSE PHYSICIAN (pre-registration) required immediately.

Applications to the Hospital Secretary, together with 2 copies of testimonials.

**HENLEY-ON-THAMES, OXFORDSHIRE. PEPPARD** CHEST HOSPITAL. (236 Beds.) READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of JUNIOR HOSPITAL MEDICAL OFFICER, vacant 28th April, 1958. The Hospital deals with all types of chest disease in medical and surgical wards. Previous experience in resident hospital appointments is desirable. Single accommodation is available.

Applications, stating age, qualifications and experience, with the names of 2 referees, should be forwarded to the Group Secretary, Reading and District Hospital Management Committee, 3, Craven-road, Reading.

**HEREFORD COUNTY HOSPITAL. (341 Beds.) House** OFFICER (surgery) required immediately. Pre-registration post. Hospital recognised for F.R.C.S.

Applications, with copies of 2 recent testimonials, to Medical Superintendent, County Hospital.

**HEREFORD GENERAL HOSPITAL. (154 Beds.) House** OFFICER (general surgery) required immediately. Pre-registration post. Hospital recognised by R.C.S. Duties include care of general surgical beds and in addition for 3 months of orthopædic beds and for 3 months of E.N.T. beds.

Applications, with copies of 2 testimonials, to be sent to the Group Secretary, Victoria House, Eign-street, Hereford.

**HILLINGDON HOSPITAL, Uxbridge, Middlesex. (621** Beds.) REGISTRAR in General and Traumatic Surgery. Candidates may visit Hospital by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Uxbridge Group Hospital Management Committee, The Furze, Pield Heath-road, Uxbridge, Middlesex, by 2nd May.

**HUDDERSFIELD. ST. LUKE'S HOSPITAL. (235 Beds.)** HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Senior House Officer grade) at the above Hospital, to commence duties immediately. The duties will be mainly surgical, in a hospital which caters for chronic sick, children, maternity, and acute medical and surgical patients. Salary in accordance with the terms and conditions of service for hospital medical and dental staff, £819 10s. p.a.

Applications, together with copies of 3 recent testimonials, to be sent to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

**HUNTINGDON COUNTY HOSPITAL. Applications are** invited for the post of HOUSE OFFICER (surgical), now vacant. Post recognised for pre-registration purposes.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

**ILFORD. KING GEORGE HOSPITAL, Eastern-avenue.** There will be a vacancy for a HOUSE PHYSICIAN at above Hospital on 26th May, 1958. First or second post pre-registration. The post will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary,
Ilford and Barking Group Hospital Management Committee.

**ILFORD. KING GEORGE HOSPITAL, Eastern-avenue.** There will be the following vacancies for HOUSE SURGEONS at above Hospital:—

First or second post pre-registration, 19th May.
Second post pre-registration, 1st June.
First or second post pre-registration, 2nd June.
All posts will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary,
Ilford and Barking Group Hospital Management Committee.

**IPSWICH AND EAST SUFFOLK HOSPITAL (Heath**ROAD WING), IPSWICH. (280 Beds.) HOUSE PHYSICIAN (pre-registration). Post vacant 6th June.

Applications, with copies of 3 recent testimonials, to Secretary.

**IPSWICH AND EAST SUFFOLK HOSPITAL (Heath**ROAD WING), IPSWICH. Pre-registration post of HOUSE SURGEON to General Surgeon vacant. Recognised for R.C.S. examination.

Applications, with copies of recent testimonials, to Hospital Secretary.

**KETTERING AND DISTRICT GENERAL HOSPITAL,** NORTHAMPTONSHIRE. Applications are invited for the post of Locum HOUSE SURGEON (pre-registration), from 1st April for 2 months. Post recognised for F.R.C.S.

Applications, stating age, experience, and qualifications, together with copies of 3 recent testimonials, to be sent to the Group Secretary at the above address.

**KINGSTON HOSPITAL, Wolverton-avenue, Kingston-**ON-THAMES. Applications are invited from suitably qualified and experienced Medical Officers for the post of REGISTRAR (anæsthetics)—full-time—at the above Hospital.

Forms of application are obtainable from the Group Secretary, Kingston Group Hospital Management Committee, 35, Coombe-road, Kingston-on-Thames, and the completed forms should be returned to him within 14 days of the appearance of this advertisement.

**LANCASTER. BEAUMONT HOSPITAL, Slyne-road.** PÆDIATRIC REGISTRAR (resident). Experience essential of all practical pædiatric techniques (exchange transfusion, blood-transfusion, &c.). Duties include experience in children's medical ward, in neonatal unit, and pædiatric outpatient clinics. Unit recognised for D.C.H. Candidates may visit Hospital by direct appointment.

Applications, together with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster.

**LANCASTER MOOR HOSPITAL, LANCASTER.** (Regional Mental Hospital.) Applications are invited for the post of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER, Male or Female. Furnished quarters for single candidate or furnished flat for married candidate. The Hospital serves North Lancashire and the Lake District, is recognised for the D.P.M., and all facilities will be given for taking this examination. All modern methods of investigation and treatment are carried out and opportunity will be given to successful candidates to attend outpatients and become acquainted with up-to-date psychological and electroencephalographic investigations. The post is for an initial period of 4 years but renewable if service is satisfactory.

Apply to Medical Superintendent, giving names of 2 referees, within 2 weeks of the appearance of this advertisement.

**LEEDS REGIONAL HOSPITAL BOARD. Registrar** vacancies.

*Anæsthetics*

St. James's Hospital, Leeds (approximately 500 surgical Beds). Recognised for F.F.A. R.C.S. Resident.

*Chest Diseases*

Castle Hill Sanatorium, Cottingham, near Hull, E. Yorks (220 Beds). Person appointed will also work in close association with the Thoracic Surgical Unit at Castle Hill, the Hull Chest Clinic and the Mass Radiography Unit. Single or married accommodation available.

*Infectious Diseases*

Castle Hill Hospital, Cottingham (167 infectious diseases beds).

*General Medicine*

(*a*) Halifax General Hospital (110 general medical beds). Resident.

(*b*) Pontefract and Castleford Group (65 general medical beds). Married accommodation available.

(*c*) Scarborough, Bridlington, Malton and Whitby Group (67 medical beds). Furnished cottage available at an economic rent.

*Obstetrics and Gynæcology*

St. Luke's Hospital, Bradford (118 obstetric and 105 gynæcological beds). Recognised for M.R.C.O.G. Resident.

*Pædiatrics*

Victoria Hospital for Sick Children, Hull, and other general hospitals with pædiatric beds in the Hull A and East Riding Hospital Management Committee Groups (aggregate 150 Beds). Non-resident.

*Psychiatry*

Scalebor Park Hospital (300 Beds). Annual admission-rate approximately 450. Accommodation available for single person. Facilities for attendance at Leeds University will be provided if the successful candidate is studying for the D.P.M.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 30th April, 1958.

**LEEDS REGIONAL HOSPITAL BOARD. Senior Regis-**TRAR vacancies.

*Anæsthetics*

Hull A Group of hospitals with additional duties as required in the Hull B and East Riding Groups. Non-resident.

*Infectious Diseases*

Seacroft (Infectious Diseases) Hospital, Leeds (200 infectious diseases beds with a high average occupancy). The post will be resident, and previous experience in infectious diseases is essential.

*Orthopædic Surgery*

Bradford A and B Groups with duties mainly at Bradford Royal Infirmary and at Woodlands Orthopædic Hospital, Rawdon.

*Otolaryngology*

Royal Eye and Ear Hospital, Bradford (67 E.N.T. beds in the Group).

*Pathology*

Bradford A and B Groups. Non-resident.

*Psychiatry*

St. James's Hospital, Leeds (General Hospital Psychiatric Unit). Candidates must hold the D.P.M. or equivalent qualification. This appointment offers excellent opportunity for experience in dealing with neurosis. The work will be in association with the University Department of Psychiatry, research and teaching may be undertaken.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 7th May, 1958.

**LEEDS. UNITED LEEDS HOSPITALS/LEEDS REG-**IONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR in Psychiatry associated with the Leeds University Department of Psychiatry. The successful candidate will undertake duties in connection with the clinical, teaching and research work of the Department at the General Infirmary and St. James's Hospital, Leeds. Candidates should hold high medical qualifications and a Diploma in Psychological Medicine or equivalent.

Applications, stating age, qualifications and details of appointments held, showing dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 7th May, 1958.

**LEICESTER ISOLATION HOSPITAL AND CHEST** UNIT, Groby-road, LEICESTER. (328 Beds.) Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (surgical). Salary £819 10s. p.a. less £150 residential emoluments. The appointment is tenable for 6 months, and may be extended for a further period of 6 months. Experience will be gained in all branches of thoracic surgery, including cardiac surgery. The post is recognised for the Final Fellowship.

Applications, giving age, qualifications, dates, &c., and copies of 2 recent testimonials, to be forwarded as soon as possible to the Department of Thoracic Surgery at the above Hospital.

**LINCOLN. HARMSTON HALL HOSPITAL. (345 Beds.)** SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (psychiatry) required immediately for above Mental Deficiency Institution. Facilities for postgraduate study in conjunction with Sheffield University available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 28th April, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

**LINCOLN. ST. GEORGE'S HOSPITAL. (242 Beds.)** LINCOLN NO. 1 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE PHYSICIAN at the above Hospital, vacant from 1st May. Duties include acute medical, acute chest and pædiatrics.

Applications, giving full particulars and names for reference, should be addressed to the Secretary.

**LIVERPOOL, 20. BOOTLE HOSPITAL. Posts are vacant** for:—

SENIOR HOUSE SURGEON (orthopædic and general surgery).

HOUSE SURGEON. Recognised pre-registration post.

Apply to Secretary.

**MACCLESFIELD HOSPITAL (West Park Branch).** Applications invited SENIOR HOUSE OFFICER (pædiatrics). Department is a busy one of 33 Beds and 30 neonatal cots and is recognised for purpose of Diploma in Child Health and provides invaluable experience.

Apply immediately, quoting 2 referees, to Group Secretary, Macclesfield and District Hospital Management Committee, "Willerby House," Cumberland-street, Macclesfield.

**MAIDSTONE. WEST KENT GENERAL HOSPITAL.** (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Vacant now. Recognised for F.R.C.S. Salary at the rate of £467 10s.–£577 10s. p.a. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

**MALVERN. ST. WULSTAN'S HOSPITAL. (230 Beds.)** RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer) required. Good experience in modern treatment of pulmonary tuberculosis and other chest diseases.

Applications to the Physician-Superintendent.

**MORECAMBE. QUEEN VICTORIA HOSPITAL. (100** Beds.) RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer grade). Post tenable for 1 year.

Applications, with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster.

**MANCHESTER. CRUMPSALL HOSPITAL.** Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade). Now vacant. Tenable for 1 year and presents opportunities for gaining experience in all branches of clinical pathology. Previous experience in pathology not essential.

Applications, with full details, and names of 2 referees, by 28th April, 1958, to Group Secretary, North Manchester Hospital Management Committee, Crumpsall Hospital, Manchester, 8.

**MANCHESTER. UNITED MANCHESTER HOSPITALS.** MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of SENIOR RESIDENT HOUSE OFFICER.

Application forms may be obtained from H. R. NORTH, General Superintendent, Manchester Royal Eye Hospital.

**MANCHESTER, 20. WITHINGTON HOSPITAL. South** MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (obstetrics and gynæcology) becoming vacant on 8th May, 1958. The Hospital takes part in undergraduate medical teaching, and the post is recognised in obstetrics and gynæcology for M.R.C.O.G. purposes.

An application form should be obtained from the Group Secretary at the Hospital and returned within 14 days of the appearance of this advertisement.

**MANCHESTER REGIONAL HOSPITAL BOARD. Regis-**TRAR in General Medicine to the Bolton and District Group of hospitals, with main duties at Bolton District General Hospital and Bolton Royal Infirmary.

Applications, stating age, nationality, qualifications, experience and the names of 2 referees, should be sent immediately to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton.

**MANCHESTER REGIONAL HOSPITAL BOARD** invites applications for post of resident or non-resident SURGICAL REGISTRAR to Macclesfield District Group of hospitals, main duties Infirmary Branch Macclesfield Hospital. Hospital recognised under F.R.C.S. regulations.

Apply immediately, with names and addresses of 2 referees, to Group Secretary, Willerby House, Cumberland-street, Macclesfield.

**MIDDLESBROUGH GENERAL HOSPITAL, Ayresome** Green-lane, MIDDLESBROUGH. (305 Beds.) SOUTH TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of HOUSE OFFICER (general surgery) at the above Hospital. The post is recognised for pre-registration service under the Medical Act, 1950, and is now vacant.

Applications, stating full details and giving 2 names for reference, should be addressed to the Hospital Secretary at the above address.

**NEWARK GENERAL HOSPITAL. Nottingham No. 1** HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER (medical) required for above Hospital situated on Great North-road, approximately 20 miles from Nottingham. Post offers good experience. Consultant staff attending Newark Hospital are on 1 or more of the Nottingham Hospitals. Flat available as married quarters. Salary and conditions of service in accordance with Ministry regulations. Duties to commence about 29th April, 1958.

Applications, giving names of 3 referees, should be sent to Group Secretary, Nottingham No. 1 Hospital Management Committee, General Hospital, Nottingham.

**NEWCASTLE REGIONAL HOSPITAL BOARD.** REGISTRAR PHYSICIAN, whole-time, for North West Durham Group of hospitals—main hospital Shotley Bridge General (325 Beds). Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

**NEWCASTLE REGIONAL HOSPITAL BOARD.** REGISTRAR SURGEON, whole-time, resident, for Gateshead Group of hospitals. Main hospital Dunston Hill (296 Beds). Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

**NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS.** Applications are invited for the post of REGISTRAR in the Department of Obstetrics and Gynæcology. The successful candidate will have duties in the Royal Victoria Infirmary (resident or non-resident) and the Princess Mary Maternity Hospital (resident). The appointment is recognised for examination purposes by the Royal College of Obstetrics and Gynæcologists. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Newcastle upon Tyne.

**NEWTON ABBOT HOSPITAL. (General section, 65 Beds.)** RESIDENT SENIOR HOUSE SURGEON, Male or Female, required approximately end May, 1958. Married quarters available.

Applications, quoting Ref. F.364/40, stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, South Devon.

**NORTHWOOD, MIDDLESEX. MOUNT VERNON HOSPITAL.** NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR required for Centre for Plastic Surgery at above Hospital. The post is for one year in the first instance and is subject to confirmation at the end of the first 6 months. Applicants must have had very good general surgical experience, and an interest in research is desirable. The Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to the Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 29th April, 1958.

**NOTTINGHAM CITY HOSPITAL. (611 Beds.)** Applications are invited for the post of HOUSE SURGEON, vacant 4th May, 1958. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

**NOTTINGHAM. HIGHBURY HOSPITAL, Bulwell, Nottingham.** SENIOR HOUSE OFFICER (medical), resident, required. Duties to commence on 23rd May, 1958. The successful candidate will, in addition to medical duties, have an opportunity of assisting in the obstetric unit. This post will be accepted as a general medical appointment entry to the M.R.C.O.G. examination.

Apply in writing, stating age, qualifications and experience, together with copies of testimonials, to the Hospital Secretary.

**PAISLEY. ROYAL ALEXANDRA INFIRMARY. Junior** HOSPITAL MEDICAL OFFICER required for Orthopædic Unit at above Infirmary.

Applications to Group Medical Superintendent.

**PLYMOUTH. SOUTH DEVON AND EAST CORNWALL** GENERAL HOSPITAL GROUP. Department of Obstetrics and Gynæcology. RESIDENT OBSTETRICAL AND GYNÆCOLOGICAL OFFICER for 1 year in the first instance; salary £935. Renewable for a second year; salary £1061 10s. Vacant 9th June, 1958. Recognised for the M.R.C.O.G.

Applications, stating age, nationality, qualifications and experience, with names of 3 referees, to be sent to the Group Secretary, 7, Nelson-gardens, Devonport, not later than 26th April, 1958.

**PLYMOUTH, SOUTH DEVON AND EAST CORNWALL** GENERAL HOSPITAL GROUP. Area Pathological Department. Applications invited from duly qualified and registered medical practitioners for the appointment of RESIDENT SENIOR HOUSE OFFICER in Pathology. The post is recognised for non-university experience for D.Path., Royal College of Physicians and Surgeons. The appointment will be for a period of 12 months, in the Area Laboratory at the South Devon and East Cornwall Hospital, Greenbank-road, Plymouth, which provides excellent modern working facilities.

Applications, stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees, to be sent as soon as possible to Group Secretary, 7, Nelson-gardens, Stoke, Plymouth.

**PLYMOUTH. SOUTH DEVON AND EAST CORNWALL** HOSPITAL, FREEDOM FIELDS. Central Casualty Department. RESIDENT SENIOR HOUSE OFFICER in Casualty, vacant immediately. Recognised for the F.R.C.S.

Applications, with names of 3 referees, to be sent to the Group Secretary.

**PLYMOUTH. SOUTH DEVON AND EAST CORNWALL** HOSPITAL. SENIOR HOUSE OFFICER in Medicine, vacant 11th June, 1958.

Applications, with names of 3 referees, to Group Secretary, 7, Nelson-gardens, Devonport.

**PLYMOUTH. SOUTH DEVON AND EAST CORNWALL** HOSPITAL, Greenbank-road. HOUSE SURGEONS, pre-registration posts, vacancies 1st and 6th June, also 1st July, 1958. Recognised for the F.R.C.S.

Applications, with full particulars, to the Group Secretary.

**POOLE GENERAL HOSPITAL, Poole, Dorset.** BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. 2 HOUSE SURGEONS required. The posts, which become vacant on 11th May and 1st June, are recognised for the F.R.C.S., F.R.C.S. (Ed.), and for pre-registration purposes.

Applications to the Hospital Secretary.

**PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.**

(1) **Saint Mary's Hospital**

HOUSE SURGEON (pre-registration). Vacant now (2 posts).

(2) **Royal Portsmouth Hospital**

(*a*) HOUSE SURGEON (pre-registration). Vacant now.

(*b*) SENIOR HOUSE OFFICER required in Orthopædic Department (104 Beds). Vacant now.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

**ORPINGTON HOSPITAL, Orpington, Kent. Resident** SENIOR HOUSE OFFICER ANÆSTHETIST required for large general hospital. Male or Female. Recognised for D.A.

Applications, with copies of 2 recent testimonials, to Surgeon-Superintendent immediately.

**OXFORD REGIONAL HOSPITAL BOARD. Registrar** in Anæsthetics to the Banbury Hospitals. Vacant now. Recognised for F.F.A. R.C.S. The appointment is for 1 year in the first instance and eligible for extension to a second year.

Applications, on forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, should reach him by 2nd May.

**READING. BATTLE HOSPITAL. (391 Beds.) Reading** AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration) required in the Accident and Orthopædic Department. F.R.C.S. recognised. Also casualty duties.

Apply, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, to Secretary.

**READING COMBINED HOSPITALS. Area Department** OF OBSTETRICS AND GYNÆCOLOGY. (100 Beds.) Applications invited from registered medical practitioners for resident post of HOUSE SURGEON. Post vacant. The appointment, recognised for M.R.C.O.G., is for 1 year, with 6 months' gynæcology at Royal Berkshire Hospital, and 6 months in Maternity Unit at Battle Hospital.

Write, stating age, qualifications with dates, nationality and present post, with copy of recent testimonial, to Secretary, Royal Berkshire Hospital, Reading.

**READING. ROYAL BERKSHIRE HOSPITAL. (339 Beds.)** Applications are invited from registered medical practitioners (Male or Female) for the post of RESIDENT SENIOR HOUSE OFFICER (anæsthetics). Vacant 1st May, 1958, for a period of 1 year. Post recognised for F.F.A. R.C.S.

Write, stating age, qualifications with dates, nationality and present post, together with names of 3 referees, to Group Secretary, Reading and District Hospital Management Committee, 3, Craven-road, Reading.

**READING. ROYAL BERKSHIRE HOSPITAL.** Applications are invited from registered medical practitioners for the post of RESIDENT ASSISTANT PATHOLOGIST (1 of 2), vacant on 15th April, 1958, and tenable for 6 months. Salary £577 10s. p.a.

Write, stating age, qualifications with dates, nationality and present post, with copies of 2 recent testimonials, to Secretary.

**READING. ROYAL BERKSHIRE HOSPITAL. (307** Beds.) Applications are invited from registered and provisionally registered medical practitioners for resident post of HOUSE SURGEON, vacant 9th April, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

**ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.)** RESIDENT HOUSE SURGEON (Male) required immediately. Not pre-registration appointment.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

**ROCHESTER, KENT. ST. BARTHOLOMEW'S HOSPITAL.** MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer grade) (1 of 2 in the department). Post vacant now and tenable for 6 months or 1 year. Recognised for F.R.C.S. Salary £819 10s. p.a.

Applications, stating age, nationality, qualifications and experience, with recent testimonials, to Hospital Secretary.

**RYDE, I.W. ROYAL I.W. COUNTY HOSPITAL. Senior** HOUSE OFFICER required as Assistant Casualty/Orthopædic Officer for approximately 4 months from 11th May.

Applications, with names of 2 referees, to Hospital Secretary by 29th April, 1958.

**SALISBURY GENERAL HOSPITAL. Temporary** CASUALTY OFFICER (Senior House Officer) required from 1st June to 18th August, 1958.

Applications, with names and addresses of 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

**SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD.** Dundee and Angus Area. Geriatrics. Applications are invited for the post of SENIOR REGISTRAR in the Geriatric Service for Dundee and Angus. The post is based at Maryfield Hospital, Dundee, a general teaching hospital of 370 Beds associated with the University of St. Andrews. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 3rd May, 1958.

**SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the post of SENIOR REGISTRAR in General Medicine on the staff of the Aberdeen General Hospitals.

Applications, giving the names of 2 referees, should be submitted by 3rd May, 1958, to the Senior Administrative Medical Officer, 1, Albyn-place, Aberdeen, from whom further particulars and a form of application may be obtained.

**SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the post of SENIOR REGISTRAR in Diagnostic Radiology with main duties in Aberdeen General Hospitals.

Applications, giving the names of 2 referees, should be submitted by 3rd May, 1958, to the Senior Administrative Medical Officer, 1, Albyn-place, Aberdeen, from whom further particulars and a form of application may be obtained.

**SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD.** REGISTRAR in E.N.T. Surgery, Royal Infirmary, Edinburgh, vacant on 19th May.

Apply, giving particulars of age, qualifications and experience, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 5th May.

**SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the appointment of REGISTRAR in Child Psychiatry based on the Department of Child Psychiatry at the Royal Hospital for Sick Children, Glasgow, which will be for 1 year in the first instance.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 26th April, 1958.

**SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the appointment of REGISTRAR in Medicine based on the Medical Unit, Gartloch Hospital, Gartcosh, Glasgow, which will be for 1 year in the first instance.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 3rd May, 1958.

**SHEPPEY GENERAL HOSPITAL, Minster, Isle of Sheppey.** MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN. Applications are invited for this pre-registration post, vacant now. Salary £467 10s.–£577 10s. p.a., according to experience.

Applications, stating age, qualifications, and experience, to the Hospital Secretary.

**SHEFFIELD, 5. CITY GENERAL HOSPITAL. Locum** SENIOR HOUSE OFFICER (orthopædics) required for the period up to 14th July, 1958. Rate of pay £15 19s. per week.

Apply, giving full details, to the Group Secretary, Sheffield No. 1 Hospital Management Committee, Nether Edge Hospital, Sheffield, 11.

**SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS AND THE SHEFFIELD REGIONAL HOSPITAL BOARD.** Applications invited for 2 posts of SENIOR REGISTRAR in Clinical Pathology. Possession of a higher qualification desirable but not essential. Appointments for 1 year in the first instance and reviewed annually. The appointments, if extended for the full period, will be divided, subject to satisfactory work and progress, between the United Sheffield Hospitals and a hospital in the area of the Sheffield Regional Hospital Board (at present the Derbyshire Royal Infirmary).

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent not later than 30th April, 1958, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

**SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL HOSPITAL.** Applications invited for the post of SURGICAL REGISTRAR at the above Hospital. The post will be held on a rotation basis between a general surgical firm and the Orthopædic Department, and it is intended that an equal period will be spent in each unit. The post offers experience in genitourinary surgery.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent not later than 26th April to the Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1.

**SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL HOSPITAL.** Applications invited for the post of RESIDENT SENIOR HOUSE OFFICER in Clinical Pathology. Pathological experience not essential, but candidates must have previous clinical experience. The successful candidate will work in turn in the different branches of clinical pathology in the laboratories of the United Sheffield Hospitals.

Applications, with the names of 3 referees or copy testimonials, should be sent to the Superintendent, Royal Hospital, West-street, Sheffield, 1, immediately.

**SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL.** (500 Beds.) HOUSE SURGEON. Vacant 1st May, 1958. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

**SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL.** (500 Beds.) HOUSE SURGEON. Vacant 23rd April, 1958. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

**SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL.** HOUSE OFFICER required in Department of Obstetrics and Gynæcology to work with part-time Registrar. Post not recognised for D.Obst.R.C.O.G.

Applications, with names of 2 referees, to Secretary.

**SOUTHAMPTON CHILDREN'S HOSPITAL. (Recognised by Conjoint Board for D.C.H.)** HOUSE OFFICER required. Total establishment of 3 residents. Salary, &c., as nationally advocated.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

**SOUTHAMPTON GENERAL HOSPITAL. (469 Beds.)** RESIDENT HOUSE OFFICER required in General Medicine with some Neurological beds. Pre-registration candidates eligible.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

**SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.** Applications are invited for an appointment as Whole-time REGISTRAR in Psychiatry to fill a vacancy in the approved trainee establishment at the Hailsham Group of hospitals, for duty at Hellingly Hospital, Hailsham, Sussex. Previous experience in general medicine is desirable. Accommodation will be available for a married practitioner. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 3rd May, 1958.

**SOUTHEND. GENERAL HOSPITAL. (262 Beds.)** Applications are invited for 2 posts of HOUSE PHYSICIAN (pre-registration), vacant 1st and 16th June, 1958.

Applications, stating age, qualifications, experience, &c., together with copies of recent testimonials, should reach the undersigned at the hospital by 1st May, 1958.

J. C. FIELD, Secretary.

**SOUTHEND. GENERAL HOSPITAL. (262 Beds.)** Applications are invited from registered or provisionally registered practitioners for 2 posts as RESIDENT HOUSE SURGEON. 1 post now vacant; second post vacant 4th June, 1958.

Applications, stating age, qualifications and previous experience, with copies of recent testimonials (1 testimonial sufficient from applicants for first appointment), should reach the undersigned by 1st May, 1958. J. C. FIELD, Secretary.

**ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire.** (384 Beds.) HOUSE SURGEON (House Officer grade) required for 1 of the 2 surgical teams. Post recognised for F.R.C.S. Post vacant now, and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

**ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire.** (384 Beds.) Locum Tenens ANÆSTHETIC REGISTRAR (resident), required from 9th to 16th May inclusive. Post recognised for F.F.A. R.C.S. and D.A.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

**ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire.** (384 Beds.) Locum Tenens SURGICAL REGISTRAR, resident, required for 1 of the 2 surgical teams from 17th to 25th May, 1958, inclusive.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Hertfordshire.

**STOKE-ON-TRENT. CITY GENERAL HOSPITAL.** (815 Beds.) HOUSE OFFICER (general surgery) required. Vacant shortly. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to the Secretary at the Hospital.

**STOKE-ON-TRENT. CITY GENERAL HOSPITAL.** Applications invited for HOUSE OFFICER (medical), vacant shortly. Recognised pre-registration post.

Detailed applications to the Secretary at the Hospital.

**STOKE-ON-TRENT. CITY GENERAL HOSPITAL.** SENIOR HOUSE OFFICER (obstetrics and gynæcology) required. Post vacant during May. Recognised D.Obst.R.C.O.G.

Detailed applications to Hospital Secretary as soon as possible.

**STOKE-ON-TRENT. NORTH STAFFORDSHIRE** ROYAL INFIRMARY. HOUSE OFFICER (general surgery) required. Recognised for F.R.C.S. Post vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, as soon as possible.

**STOKE-ON-TRENT. NORTH STAFFORDSHIRE** ROYAL INFIRMARY. SENIOR HOUSE OFFICER (anæsthetics) required. Post recognised for F.F.A. R.C.S. and D.A. Medical library facilities available.

Detailed applications to Hospital Secretary as soon as possible.

**STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.)** STOCKPORT AND BUXTON HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (anæsthetics), vacant 16th May, 1958. The post is recognised for the D.A. and F.F.A. R.C.S., and there are facilities for study.

Applications, stating age, experience and qualifications, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw Heath, Stockport.

**STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.)** Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics). The post, which may be either resident or non-resident, becomes vacant on 1st June, 1958.

Applications, stating age, qualifications and experience, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

**TAPLOW, near MAIDENHEAD. CANADIAN RED** CROSS MEMORIAL HOSPITAL. REGISTRAR required to the Special Unit for Research in Juvenile Rheumatism. Post offers scope for those interested in research, pædiatrics, rheumatology or cardiology.

Application forms from and returnable to Secretary, Windsor Hospital Management Committee, Alma-road, Windsor, by 30th April.

**TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS** MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant immediately. Pre-registration post.

Applications, stating age, qualifications, with dates, with copies of 2 testimonials, to Secretary.

**TAUNTON AND SOMERSET HOSPITAL. Applications** are invited for the post of SENIOR HOUSE OFFICER (obstetrics and gynæcology). Vacant 11th May, 1958. The department consists of the Area Maternity Unit of 50 Beds (recently modernised and extended) and a Gynæcological Ward of 25 Beds. Recognised for the M.R.C.O.G.

Applications, stating age, qualifications, nationality and experience, together with the names of 2 referees, should be forwarded immediately to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset.

**TAUNTON AND SOMERSET HOSPITAL. Applications** are invited for HOUSE OFFICER (E.N.T.) post. Vacant now. Post-registration appointment, recognised for F.R.C.S. and D.L.O.

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded immediately to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset.

**TUNBRIDGE WELLS (near). PEMBURY HOSPITAL,** PEMBURY. Applications invited for appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON AND CASUALTY OFFICER (Senior House Officer grade) to begin duties as soon as possible. Recognised F.R.C.S. (Eng.) and tenable for 1 year. Work includes treatment of long- and short-stay cases and traumatic surgery with large Outpatient and Fracture Clinics under 2 Consultants.

Apply, stating age, qualifications and experience, together with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

**WARRINGTON INFIRMARY. (172 Beds.) Applications** are invited from Males or Females for the post of RESIDENT HOUSE PHYSICIAN (pre-registration or Senior House Officer). Salary will be £467 10s.–£577 10s. p.a., less a deduction of £125 for full residential emoluments, or Senior House Officer grade £819 10s. p.a., less £150 for residential emoluments.

Applications should be forwarded to HENRY L. BOOT, Group Secretary, Warrington and District Hospital Management Committee, c/o General Hospital, Warrington, Lancs.

**WATFORD, HERTFORDSHIRE. PEACE MEMORIAL** HOSPITAL. (211 Beds.) CASUALTY OFFICER (Senior House Officer) required. Modern Department employing 3 full-time Casualty Officers including whole-time Surgeon-in-charge. Post recognised for F.R.C.S. Resident or non-resident. Post vacant beginning of May.

Please send applications, with copies of 2 references, to the Administrator.

**WEYMOUTH HOSPITALS. West Dorset Group Hos-**PITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR (Registrar grade) required; based at Weymouth and District Hospital. Post tenable for 12 months, with possible renewal for further year. Salary according to experience—£935 or £1061 10s. p.a., with deduction of £170 p.a. if resident.

Application form, returnable immediately, from Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset.

**WEYMOUTH AND DISTRICT HOSPITAL. Locum** MEDICAL REGISTRAR (Registrar grade) (Male or Female) required from 1st May. Salary £19 5s. per week. Residence available if necessary.

Applications, stating age, qualifications, experience and enclosing copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

**WEYMOUTH AND DISTRICT HOSPITAL. (124 Beds.)** HOUSE SURGEON (Male or Female) required for resident pre-registration post. Recognised for F.R.C.S. examination and tenable for 6 months.

Applications, stating age, qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

**WELSH REGIONAL HOSPITAL BOARD. Registrar** (plastic surgery), St. Lawrence Hospital, Chepstow (182 Beds). Expected to visit other hospitals in South Wales area. Considerable opportunities for training in specialty. Accommodation for single person. Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

**WESTCLIFF HOSPITAL, Balmoral-road, Westcliff-**ON-SEA, ESSEX. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Senior House Officer grade). Post vacant 1st June, 1958. The Hospital covers a wide field of medicine and offers excellent training for general practice.

Applications should be sent to the Secretary, General Hospital, Prittlewell Chase, Southend-on-Sea, Essex, not later than 1st May, 1958.

**WHITEHAVEN HOSPITAL, Cumberland. (119 Beds, pre-**registration post, recognised F.R.C.S.(Ed.).) HOUSE SURGEON (first, second, or Senior House Officer post). Vacant beginning of April.

Detailed applications with dates, and names of 2 referees, to Secretary, Workington Infirmary, Cumberland.

**WIGAN AND LEIGH HOSPITAL MANAGEMENT COM-**MITTEE. ASTLEY HOSPITAL, ASTLEY, near MANCHESTER. SENIOR HOUSE OFFICER in Surgery required. Duties include gynæcology and casualty. Resident post. Vacant now.

Apply Secretary, Knowsley House, Wigan.

**WIGAN AND LEIGH HOSPITAL MANAGEMENT** COMMITTEE. SURGICAL REGISTRAR, resident, required at Royal Albert Edward Infirmary, Wigan. Preference given to holders of higher surgical qualifications. Post recognised for F.R.C.S.

Apply, with names of 2 referees, to Secretary, Royal Albert Edward Infirmary, Wigan.

**WILLERBY, EAST YORKSHIRE (near Hull). DE LA** POLE HOSPITAL. (1174 Beds—mental illness and nervous disorders.) JUNIOR HOSPITAL MEDICAL OFFICER. Modern reception hospital, villas and neurosis unit. All modern methods of treatment practised. Accepted for D.P.M. training.

Application forms from Group Secretary, Hull B Hospital Management Committee, at the above address.

**WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-**PITAL. (327 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant immediately.

Applications, with copies of 2 testimonials, to Group Secretary.

**WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-**PITAL. (327 Beds.) HOUSE SURGEON to the Senior Surgeon. Post vacant end April.

Applications, with copies of 2 testimonials, to the Group Secretary.

**WINDSOR. KING EDWARD VII HOSPITAL. Registrar** (Casualty Officer), resident, required immediately. There is an Accident Unit of 30 Beds at the Hospital and with the Casualty Department forms part of the Accident Service for the Windsor Group and includes duties with the E.N.T. and Eye Departments. Candidates should have had previous experience in the treatment of acute injuries.

Application forms from and returnable to Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor.

**WOLVERHAMPTON. THE ROYAL HOSPITAL. (An** associated hospital of the Birmingham University Medical School.) ORTHOPÆDIC SENIOR HOUSE SURGEON for Fracture and Orthopædic Department. Post recognised for F.R.C.S. Vacant immediately.

Apply, with 2 testimonials, to the Secretary.

**WORCESTER. RONKSWOOD HOSPITAL. (312 Beds.)** SENIOR HOUSE OFFICER (surgical) required immediately at this busy general hospital, which is associated with Worcester Royal Infirmary. The appointment offers wide and varied experience and is recognised for the F.R.C.S. examination.

Applications to Hospital Secretary.

**WORKINGTON INFIRMARY, Cumberland. (155 Beds,** pre-registration post, recognised F.R.C.S.(Ed.).) HOUSE SURGEON (first, second or Senior House Officer post).

Detailed applications with dates, and names of 2 referees, to Secretary.

**WORTHING GROUP HOSPITAL MANAGEMENT COM-**MITTEE AND CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the new appointment of REGISTRAR in Physical Medicine to be made jointly by the bodies concerned. The post will entail working in both the Worthing and Chichester Groups, and the successful candidate will work under the Consultant in Physical Medicine. This post is recognised for Part II of the Diploma of Physical Medicine.

Application forms are obtainable from the undersigned, and should be returned within 21 days of the appearance of this advertisement. A. V. OAKTON, Group Secretary.

Worthing Group Hospital Management Committee,
129, Brighton-road, Worthing, Sussex.

**NORTHERN IRELAND HOSPITALS AUTHORITY.** Applications are invited for 8 Whole-time posts as SENIOR HOUSE OFFICER in Clinical Pathology for the year commencing 1st August, 1958. The terms and conditions will be in accordance with the Authority's application of the Spens report to Northern Ireland.

Applications to be made on a form obtainable (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and to be returned not later than 28th April, 1958.

**NORTHERN IRELAND HOSPITALS AUTHORITY.** Applications are invited for whole-time posts as JUNIOR TUTOR/SENIOR HOUSE OFFICER at teaching hospitals in Belfast for the year commencing 1st August, 1958. The appointments will be made jointly by the Queen's University, Belfast, and the Authority, and will involve teaching and other University duties as Junior Tutor.

Vacancies will occur in the following departments :—

| | |
|---|---|
| Child Health | Medicine |
| Midwifery and Gynæcology | Surgery |

Applications should be made on a form which may be obtained (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and which must be returned so as to be received not later than 28th April, 1958.

**NORTHERN IRELAND HOSPITALS AUTHORITY.** Applications are invited for whole-time posts as REGISTRARS AND TUTORS/REGISTRARS in hospitals in Northern Ireland for the year commencing 1st October, 1958. Vacancies will occur in all specialties, and appointments will be made in either of 2 grades, viz., Senior Registrar or Principal Registrar, the analogous grades in Great Britain being Registrar and Senior Registrar. Some of the appointments will be made jointly by the Queen's University, Belfast, and the Authority, and will involve teaching and other University duties as Senior or Principal Tutor. Vacancies for Registrars exist in several specialties at present, and applicants who would be interested in these posts should clearly indicate on their application forms the earliest date on which they would be available for duty if appointed.

Applications should be made on a form which may be obtained (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and which must be returned so as to be received not later than 28th April, 1958.

**CORK MENTAL HOSPITAL BOARD. Vacancy for** TEMPORARY RESIDENT ASSISTANT MEDICAL OFFICER. Remuneration £569 p.a. approximately.

Application forms and particulars may be obtained from the County Manager, Courthouse, Cork, with whom completed applications should be lodged not later than 5 P.M. on Friday, 25th April, 1958.

**ADDIS ABABA, ETHIOPIA. PRINCESS TSAHAI** MEMORIAL HOSPITAL. OBSTETRICS HOUSE SURGEON. Salary E$1000 a month less tax. 1 month annual leave (cumulative). Flat and furniture supplied. 3-year contract.

Application form and further details from Hon. Secretary, Princess Tsahai Memorial Hospital Council, 2, Ross-court, Putney Hill, S.W.15.

**CANADA. ST. PAUL'S HOSPITAL, Vancouver, British** COLUMBIA, CANADA. Applications are invited for 1 year JUNIOR ROTATING INTERNESHIPS at approved large general hospital. Remuneration $175 per month.

Apply Sister Superior, St. Paul's Hospital, 1081 Burrard-street, Vancouver, B.C., Canada. Canadian, American or British graduates only are acceptable.

**MICHIGAN, U.S.A. OAKWOOD HOSPITAL, Dearborn,** MICHIGAN. Applications are invited for 1 year approved ROTATING INTERNSHIP beginning 1st July, 1958. 234-Bed General Hospital 10 miles from Detroit. Excellent facilities. Hospital approved for exchange-visitor programme. Salary $200 if single, $250 if married. Housing rent-free.

Apply Director.

**TIBERIAS, ISRAEL. CHURCH OF SCOTLAND HOS-**PITAL. This hospital undertakes most of the midwifery and gynæcological work in Northern Galilee and requires a Doctor with some experience in this work. Normally, the engagement is for 5 years but, in the present emergency, a shorter engagement of from 1 to 2 years would be accorded.

Passages out and home will be paid, and the full terms of engagement can be obtained from Rev. R. CLEPHANE MACANNA, M.A., Overseas Department, 121, George-street, Edinburgh.

**U.S.A. BRIDGEPORT HOSPITAL, Bridgeport, Connecti-**CUT. Approved ROTATING INTERNSHIPS and RESIDENCIES available in a general hospital of 387 Beds and 60 Bassinets. Stipend of $190 per month in addition to full maintenance and uniforms. Exchange Visitor Program participant.

Address inquiries to: Chairman, Committee on Medical Education, Bridgeport Hospital, Bridgeport 10, Connecticut, U.S.A.

**U.S.A. UNIVERSITY OF MINNESOTA MEDICAL** CENTER. ANESTHESIOLOGY RESIDENCIES at the above Center. 2 or 3-year programme with clinical and didactic instruction in all phases of anæsthesia. Board approval. Positions starting every month.

Address, F. H. VANBERGEN, M.D., University of Minnesota Medical Center, Minneapolis 14, Minnesota.

## Public Appointments

**FACTORY DOCTORS. Factories Acts 1937 and 1948.** The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

| *District* | *County* | *Latest date for receipt of applications* |
|---|---|---|
| MIDDLESBROUGH | .. YORK .. | .. 3RD MAY, 1958 |
| CASTLEFORD .. | .. YORK .. | .. 3RD MAY, 1958 |

**HALIFAX. COUNTY BOROUGH OF HALIFAX.** Applications are invited from duly qualified medical practitioners possessing the D.P.H. for the full-time appointment of MEDICAL OFFICER OF HEALTH. The salary will be £1850 rising to £2120 p.a., and the successful applicant will not be allowed to engage in private practice.

Full particulars are available from the undersigned. Closing date for applications 28th April, 1958.

RICHARD DE Z. HALL, Town Clerk.

Town Hall, Halifax, 1st April, 1958.

**BIRMINGHAM. CITY OF BIRMINGHAM. Public** HEALTH DEPARTMENT. Applications are invited from registered medical practitioners for post of ASSISTANT ADMINISTRATIVE MEDICAL OFFICER OF HEALTH (Male or Female). Candidates should hold the Diploma of Public Health. The successful candidate will have an opportunity to gain administrative experience in all branches of the Public Health Service, including Maternity and Child Welfare. Salary scale £1405–£55–£1625 p.a. Commencing salary within the scale will depend upon the medical officer's experience. Pension scheme (including Widows and Orphans); medical examination. The officer appointed will be required to devote his/her whole time to official duties and the appointment will be subject to 3 months' notice on either side.

Applications, with names of 3 persons to whom reference may be made, to be sent to the Medical Officer of Health, Council House, Birmingham, 3, not later than 25th April, 1958.

**BUCKINGHAMSHIRE COUNTY COUNCIL. Applications** are invited from registered medical practitioners for the appointment of ASSISTANT COUNTY MEDICAL OFFICER in the South Bucks Area. Preference will be given to applicants possessing a Diploma in Public Health or a Diploma in Child Health, and experience in maternity, school medical and child welfare work. Salary within the scale £1050–£1475 p.a., the commencing salary being fixed according to qualifications and experience. Travelling and subsistence allowances on the County Council's scale will be paid. The appointment is superannuable and subject to medical examination.

Further particulars and forms of application may be obtained from the County Medical Officer, County Offices, Aylesbury, to whom completed applications must be returned by Monday, 5th May, 1958.

R. E. MILLARD, Clerk of the Bucks County Council.

County Hall, Aylesbury.

**NATIONAL COAL BOARD. NORTH WESTERN DIVI-**SION. NO. 2 (WIGAN) AREA. Applications are invited from registered medical practitioners for the post of ASSISTANT AREA MEDICAL OFFICER in the No. 2 (Wigan) Area of the North Western Division of the National Coal Board. The successful applicant will assist the Area Medical Officer in the supervision of an industrial health service, including the examination of new entrants. The work entails underground visits at collieries. Candidates should have completed hospital and other post-graduate training. Experience in general practice and an interest in the field of preventive or industrial medicine would be an advantage. Salary according to qualifications and experience, within the range £1250–£1700 p.a.

Detailed applications, giving the names of 2 referees, to the Divisional Chief Staff Officer, 40, Portland-street, Manchester, 1, within 14 days.

**NAVY, ARMY AND AIR FORCE INSTITUTES.** Applications are invited from general practitioners in the undernoted towns for the appointment in a part-time capacity as MEDICAL OFFICERS to this Corporation. Successful applicants would be required to examine and report on the condition of the employees of the Corporation who may be referred to them from time to time. Fees for this work will be paid on a scale agreed with the British Medical Association.

Applications, giving details of qualifications and experience, should be sent to the Chief Medical Officer, Navy, Army and Air Force Institutes, Kennington-lane, London, S.E.11, not later than 26th April, 1958.

The towns for which applications are invited are:—

| | | |
|---|---|---|
| CHIPPENHAM | BRISTOL | TAUNTON |
| YEOVIL | EXETER | MINEHEAD |

**MEDICAL OFFICERS**

THE UNITED KINGDOM ATOMIC ENERGY AUTHORITY, INDUSTRIAL GROUP,

requires

MEDICAL OFFICERS

at its establishment in the North of England and in Scotland.

There is, as yet, no special qualification in radiological protection, but qualifications or experience in any of the following will be an advantage:

Industrial Medicine
Radiology
Pure Science

The field of health and safety in atomic energy offers good career prospects to those who wish to specialise in either industrial medical practice or the broader aspects of radiological protection, including health physics. The Authority will provide a certain amount of initial training and it is expected that, in due course, there will be a formal training scheme which will lead to specialisation in radiological protection. Candidates for these advanced courses will normally be selected from the Medical Officers in post.

The upper salary limit for these posts is £2400.

The posts are permanent and pensionable. Housing will be available, if required.

Write, in confidence, to

Director of Personnel and Administration,
United Kingdom Atomic Energy Authority,
Industrial Group Headquarters,
Risley, Warrington, Lancashire.

Please quote reference 2370.

* Medically qualified candidates who have applied against the recent general advertisement for Health and Safety staff will be automatically considered for these posts.

Closing date: 28th April, 1958.

**COVENTRY CORPORATION** require **School Medical** OFFICER AND ASSISTANT MEDICAL OFFICER OF HEALTH (joint post) for duties connected with medical inspection and clinic treatment of schoolchildren, maternity and child welfare work, and such other duties as the Medical Officer of Health and Principal School Medical Officer may include from time to time. Qualifications/experience in ascertainment of handicapped pupils an advantage. Salary £1050–£1475. Commencing salary according to experience/qualifications. Removal loan available.

Application forms, &c., from Medical Officer of Health, New Council Offices, Coventry, returnable without delay.

**DURHAM COUNTY COUNCIL. Health Department.** ASSISTANT MATERNITY AND CHILD WELFARE MEDICAL OFFICER. Applications are invited from registered medical practitioners (female). Commencing salary £1050 p.a. rising by annual increments of £50 and £55 to £1475. Travelling expenses will be paid in accordance with the scale approved by the Whitley Council.

The appointment is subject to certain conditions, particulars of which may be obtained from the County Medical Officer of Health, Shire Hall, Durham, to whom applications, together with the names of not more than 3 referees should be sent not later than 30th April, 1958. Canvassing members of the Council is prohibited.

J. K. HOPE, Clerk of the County Council.

**LANCASHIRE COUNTY COUNCIL. Applications are** invited from registered medical practitioners for appointment as ASSISTANT DIVISIONAL MEDICAL OFFICER in the Bury (near Manchester) area. Possession of Diploma in Public Health desirable. Salary £1050 rising to £1475 p.a. Travelling and subsistence allowances where applicable.

Application forms and further particulars from County Medical Officer, Serial 757, East Cliff County Offices, Preston. Application forms to be returned by 30th April, 1958.

**SURREY COUNTY COUNCIL. Appointment of Assistant** MEDICAL OFFICERS (Male). Applications are invited from candidates possessing the D.P.H. or D.C.H. Main duties will be in connection with the school health and maternity and child welfare service. Salary according to experience, on the scale £1050–£50–£1200–£55–£1475 p.a. The appointment is subject to the provisions of the Local Government Superannuation Acts, 1937/1953, and to 3 months' notice on either side.

Application form from the County Medical Officer, County Hall, Kingston-upon-Thames, to be returned by 26th April, 1958.

**GOVERNMENT OF JAMAICA. Medical Officers with** qualifications registrable in United Kingdom required as follows:

(*a*) Doctors who have completed 1 year's House appointment to assist Medical Officer in charge of district hospital or a Specialist at Kingston Public Hospital (540 Beds) in general surgery and medicine, pædiatrics, E.N.T., eye, casualty (rotation service). "R" practitioners, i.e. practitioners liable for call-up under the National Service Acts may apply and, if appointed, will be granted indefinite deferment of call-up on completion of minimum tour of 2 years.

(*b*) Doctors with 3 or 4 years' approved experience following graduation for duties as above but with more responsibility. May also be assigned for duty in psychiatry at Bellevue (Mental) Hospital (3000 Beds).

(*c*) Doctors between 45 and 50 years of age with more than 4 years' approved experience for general duty at Kingston Public Hospital or as Medical Officer in districts to hold regular clinics and have medico-legal responsibilities and perform post-mortems.

Appointments on contract for 3 years in first instance with possibility of eventual pensionable employment. Salary scale £900–£1600 a year. Starting salary depends on experience. On satisfactory completion of service a gratuity (taxable) of 20% of salary is payable for each completed 3 months' service. (Not payable if officer is placed on pensionable establishment.) Free passages for officer, wife, and dependent children under 18 years, not exceeding 5 persons in all. Quarters not provided but subsidy payable where rents exceed 10% of salary. Income-tax at local rates. Climate healthy. Educational facilities available.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/32/023).

**WESTERN REGION OF NIGERIA. Male Medical Officer** (Psychiatrist) required in new mental hospital which will be expanded shortly to 200 Beds, with extensive outpatient attendance. Patients are drawn from large region containing diverse population with different tribal, cultural, religious background, and varying stages of social development. Candidates must possess medical qualifications registrable in United Kingdom and D.P.M.

Appointment may be:—

(*a*) on short-term contract (2 tours each of 12–24 months' duration). Salary scale £1290–£2286 a year, and gratuity (taxable) at rate of £37 10s. for each completed period of 3 months' service (including leave) payable on satisfactory completion of appointment, or

(*b*) from National Health Service, candidate retaining superannuation rights. Salary scale £1086–£1950 a year, and gratuity (taxable) of 20% of aggregate salary on completion of appointment.

In addition, officer receives supplementary pay of £120 a year, and staff pay of £100 a year.

Quarters provided at low rental. Taxes at local rates. Annual leave permissible: generous home leave after each tour. Free return passages for officer and wife. If officer is domiciled in United Kingdom return passages are payable for children under 18, provided cost does not exceed £450 (for officer domiciled elsewhere the amount will be decided by Government of Western Nigeria). Should an officer use less than maximum allowed the remainder may be used to enable wife to visit children in officer's country of domicile.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/410/029).

**WARWICKSHIRE COUNTY COUNCIL. County Medical** OFFICER OF HEALTH'S DEPARTMENT. Applications are invited from registered medical practitioners for the appointment of ASSISTANT COUNTY MEDICAL OFFICER OF HEALTH, which is in the north-eastern area of the county. Preference will be given to those holding the D.P.H. or D.C.H. and with previous experience. Conditions of service and salary (£1050–£1475) will be in accordance with the Whitley Council. The successful candidate will be required to provide a motor-car in the performance of duties, for which Whitley Council scale allowances are payable. Grant towards removal expenses will be considered.

Further particulars, including details of duties, and application forms may be obtained from the County Medical Officer of Health, Shire Hall, Warwick. Closing date for applications is 26th April, 1958.

**DONEGAL COUNTY COUNCIL. Applications are invited** for the post of Whole-time, TEMPORARY RADIOLOGIST. Candidates should hold a recognised Diploma in Diagnostic Radiology and have had at least 5 years' experience in radiology. Initial appointment will, subject to satisfactory service, be for a period of 1 year. Salary £2114 p.a. fully inclusive. Travelling expenses will be paid at approved rates for any travelling necessarily incurred on official duties.

Application forms and full particulars of the post may be had from The Secretary, Donegal County Council, Lifford, with whom completed applications must be lodged not later than 30th April, 1958.

**GOVERNMENT OF THE FEDERATION OF NIGERIA.** PATHOLOGIST required to carry out routine hæmatology, chemical pathology, morbid anatomy and to train laboratory technicians. Opportunities for individual research in clinical pathology. Experience in pathology required. Candidates must possess medical qualification registrable in United Kingdom. A higher qualification (e.g., D.C.P. or Dip. Bact.) an asset.

Appointments may be made :—

(*a*) On 3 years' probation for permanent and pensionable employment. Pension (non-contributory) at the rate of 1/600th of final pensionable emoluments for each completed month of reckonable service.

(*b*) From National Health Service, candidates retaining superannuation rights up to 6 years and receiving gratuity (taxable) of 20% of aggregate salary. Salaries under (*a*) or (*b*) £1128–£1950 p.a., or

(*c*) On short-term contract (2 tours each of 12–24 months) with salary £1338–£2286. Gratuity (taxable) of £37 10s. for each completed period of 3 months' service (including leave).

Quarters at low rental. Free return passages for officer and wife. Return passages for children, to age 18, provided this does not exceed cost of 2 adult return passages in any 1 tour of service. Children's (separate domicile) allowance of £75 a year for each child under 18, ceasing if children join parents in Nigeria. Income-tax at low local rates. Local leave permissible and generous home leave after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/14/05).

**GOVERNMENT OF THE FEDERATION OF NIGERIA.** SPECIALIST (Pædiatrician) required to take charge of a children's ward (42 Beds) and outpatient clinic at Lagos General Hospital, to act as Consultant in pædiatrics to various hospitals, to assist in building up a comprehensive child health organisation for Lagos, and to organise and take charge of the Pædiatric Department of the projected Mainland General Hospital, when built. A candidate must possess medical qualifications registrable in the United Kingdom and be a member of one of the Royal Colleges of Physicians, or F.R.F.P.S., who has specialised in pædiatrics.

Appointment :—

(*a*) On short-term contract with salary £2664 a year. On completion of contract gratuity (taxable) is paid of £37 10s. for each completed period of 3 months' service (including leave).

(*b*) From National Health Service with salary £2220 a year, candidate retaining superannuation rights and receiving gratuity (taxable) of 20% of aggregate of salary.

Quarters at low rental. Free return passages for officer and wife. Return passages for children, to age 18, provided cost does not exceed that of 2 adult return passages in any tour of service. Children's (separate domicile) allowance of £75 a year for each child under 18, ceasing if children join parents in Nigeria. Income-tax at local rates. Local leave permissible and generous home leave after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/14/048).

**GOVERNMENT OF THE EASTERN REGION OF** NIGERIA.

SPECIALIST (Pathologist) required to organise and run a Regional Laboratory Service, take charge of a Regional Laboratory when built, and administer subsidiary laboratory units attached to Government hospitals in the Region. A higher qualification is desirable.

SPECIALIST (Gynæcologist) required to undertake clinical gynæcology and obstetrics including visits to hospital units in the Region when convenient, and advising medical officers in obstetrics and gynæcology. Candidates must possess M.R.C.O.G., or equivalent, and have considerable experience.

Appointment on contract for 2 tours of not more than 2 years each. Salary £2442 a year with gratuity (taxable) on completion of satisfactory engagement at rate of £37 10s. for each completed period of 3 months' service (including leave).

Quarters provided at rental of 10% of salary. Taxes at local rates. Annual local leave; generous home leave after each tour. Free return passages for officer and wife; and, when appropriate, either (but not both) of the following in any 1 tour:—

(*a*) 1 return sea passage for each of 2 children under age of 18 subject to maximum of £75 for the return journey for each child, or

(*b*) an allowance of £75 a year for each of 2 children under age 18 maintained outside Nigeria for the whole tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/411/019).

**HER MAJESTY'S EMBASSY, WARSAW.** Medical OFFICER required. Candidates should be British by birth, under 45, and if married, preferably with not more than 1 child. Surgical as well as medical qualifications are desirable. The duties, which would be mainly clinical, are to care for the staff of Her Majesty's Embassy and their families, and also some patients from other diplomatic missions in Warsaw. The appointment is expected to carry with it a taxable salary between £830 and £1325 p.a. and a non-taxable allowance at present amounting to £525 for a single man and £915 for a married couple. Free furnished accommodation. The appointment, which would carry with it diplomatic status, would be for 1 year in the first instance.

Applications to Ministry of Labour and National Service, Professional and Executive Register (Reference PE638), Atlantic House, Farringdon-street, London, E.C.4. Only those selected for interview will be informed.

## General Practice

*For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."*

**LEYTONSTONE, London, E.11. Applications invited for** retirement VACANCY. (Urban—intermediate area.) List at present approximately 1750. Residence and surgery accommodation not available. Apply on Form E.C.16A by first post on 2nd May, 1958, to— E. BERGDAHL, Clerk of the Council.

Essex Executive Council,
131/3, Fillebrook-road, Leytonstone, E.11.

**BOURNEMOUTH. Applications invited for Vacancy** occurring 30th September (resignation). List about 1400. Intermediate area. Surgery accommodation with flat above, available for purchase. Practice has always had woman incumbent. Applications to be received by undersigned by 29th April, 1958.

R. W. LOWE, Clerk of Bournemouth Executive Council.
460, Christchurch-road, Boscombe, Bournemouth.

**EAST LINTON, EAST LOTHIAN. Applications invited** for single-handed VACANCY mainly rural, list at present 1130. Successful candidate to take over on 5th July, 1958. Opportunity will be given to purchase house by arrangement with retiring doctor. Applications by 3rd May, 1958, stating age, qualifications and experience and names of 2 referees, to Clerk, Lothians and Peebles Executive Council, 25, Stafford-street, Edinburgh, 3, from whom further information obtainable.

**MANCHESTER. Applications invited from doctors** wishing to undertake General Medical Services in Manchester. The list number of the resigning doctor is approximately 1250 and it is understood that the residence (and surgery) will be available to successor. Applications, on Form E.C.16A (obtainable from address below), must be received by the undersigned not later than first post on 28th April, 1958.

H. GLASS, Clerk of the Council.
Ardwick Town Hall, Ardwick Green North, Manchester, 12.

**NEW MILTON, HAMPSHIRE. Applications invited for** VACANCY, chiefly urban. List at present 1652. Residential and surgery accommodation available for purchase. Successful applicant will be required to take over on 5th July, 1958. Apply on form E.C.16A to Clerk, Hampshire Executive Council, 37, Southgate-street, Winchester. Completed applications to be received not later than 28th April, 1958.

**PENGE, S.E.20. Applications invited for Vacancy (Urban)** due to death. List at present approximately 1840 including approximately 27 patients who reside in Croydon. Residence and surgery likely to be available. Apply on E.C.16A before 3rd May, 1958, to— F. E. MILES, Clerk,

Kent and Canterbury Executive Council.
11, Station-road, Maidstone.

**SMETHWICK, STAFFORDSHIRE. Applications invited** for VACANCY (Urban) due to resignation of partners (husband and wife). Combined lists approximately 4050. Residence and surgery for purchase. Successor(s) to commence 1st July, 1958. Applications on E.C.16A, to be received not later than 3rd May, 1958, to the Clerk, Smethwick Executive Council, Barclays Bank Chambers, South-road, Smethwick, 41.

**WIGTON, CUMBERLAND. Applications are invited for** VACANCY (mixed Urban and Rural) owing to resignation of practitioner. List at 27th March, 1958—1700. Intermediate area. Residence and surgery available. Apply on Form E.C.16A by 25th April, 1958 to—

F. M. SMITH, Clerk to Cumberland Executive Council.
7, Chatsworth-square, Carlisle.

## Hospital Services: Non-Medical Appointments

**DUNDEE ROYAL INFIRMARY. Applications are invited** from holders of A.R.I.C., or B.Sc., preferably with honours, for appointment as HOSPITAL BIOCHEMIST (Basic grade) in the Pathology Department associated with St. Andrews University Medical School. Whitley salary.

Apply Medical Superintendent.

**HEREFORD. COUNTY HOSPITAL. Group Pathology** DEPARTMENT. Applications are invited for the post of NON-MEDICAL BIOCHEMIST (Basic grade) in the Group Pathology Department, County Hospital, Hereford.

Applications, stating age, qualifications and experience, with names of 2 referees, to the Consultant Pathologist.

**MANCHESTER. UNITED MANCHESTER HOSPITALS.** MANCHESTER ROYAL INFIRMARY. Applications are invited for the post of CHIEF TECHNICIAN II (Whitley scales). The possession of the F.I.M.L.T. or equivalent qualification is essential. Applicants must have had considerable experience in hospital laboratory administration and technology, particularly in bacteriology, and also in the control and training of technical staff.

Detailed applications to the Secretary, Manchester Royal Infirmary, Manchester, 13, by 10th May, 1958.

**EDINBURGH NORTHERN GROUP OF HOSPITALS.** Applications are invited for the post of BIOCHEMIST to conduct research in the field of rheumatic diseases. Medical qualification not essential. Salary £1000–£1200 p.a., in accordance with qualifications and experience. Appointment for 1 year in the first instance, subject to renewal.

Applications, with the names of 2 referees, to be sent to Director, Rheumatic Unit, Northern General Hospital, Ferry-road, Edinburgh, 5.

## Miscellaneous

**A large Pharmaceutical Company requires in their** Medical Department the full-time services of a Medical Practitioner (Male), age between 30 and 40 years. Preferably with a higher medical qualification and experience as Medical Registrar. The duties of this position will be primarily those of initiating and progressing clinical research investigations, although some general professional advisory work may be required. The successful applicant must be prepared to do a certain amount of travel both in the United Kingdom and abroad. Minimum salary £1750. The Company operates a non-contributory pension scheme.—Write, with fullest details, to Address No. 388, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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INDUSTRIAL MEDICAL OFFICER on the staff of the London Headquarters, responsible to the Managing Director. Duties will cover the medical examination of staff and advice on health matters at Headquarters offices and 3 of the smaller London factories. He will have a special advisory function in regard to employment in clerical, administrative, and commercial occupations.

Salary will be in accordance with the B.M.A. recommendations for such posts, with pension and life assurance cover.

Applications from qualified men with some experience, stating age, qualifications and career details, should be sent to Personnel Officer, Philips Electrical Ltd., Century House, Shaftesbury-avenue, London, W.C.2.

**MEDICAL OFFICER**

A major British Oil Company invites applications from registered Medical Practitioners (Male) for the post of Medical Officer for service in the East.

Candidates should be under the age of 35 years and, if married, accommodation and free family passages will be provided.

Pensionable starting salary in local currency is equivalent to about £2000 p.a. progressive, plus local allowances.

The contract is for 3 years in the first instance and, if renewed, generous home leave will be granted. The post is pensionable with widow's and children's benefits. Limited private practice is permitted.

Applicants will be required to produce evidence of good experience in medicine, midwifery, and especially surgery. The duties will entail charge of 1 of 3 hospitals varying in size between 50 and 200 Beds, and outpatients, to undertake associated administrative duties, and supervision of public-health services.

Write, giving brief details of qualifications and experience, to Box TL.249, c/o 191, Gresham House, E.C.2.

**Vacancies for Medical Officers in Social and Preventative** Medicine. A Welfare Organisation has vacancies in Morocco and Iran for suitably qualified medical practitioners having experience of social and preventative medicine. Contract preferably for 2 years. Senior and Junior posts available, the former carrying a total salary of approximately £3000–£3500, and the Junior posts £2400–£3000. Salaries are income-tax free, with additional benefits and allowances. Travel is paid by the Organisation. Application should be made, giving full information of experience and qualifications, with references, to Address No. 391, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

**Doctors requiring applications, theses copied: Write to** MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC. 0141), who are specialists.

**"Pregnancy Diagnosis by the Xenopus Method," 24-hour** service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

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**The British Journal of Medical Hypnotism. Quarterly,** £2 2s. p.a.—Orders to the publishers, 4, Victoria-terrace, Hove, 3, Sussex.

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